THE FIVE STAGES OF PREVENTION: 
A PRACTICAL NEW CLASSIFICATION FOR HEALTH PLANNING 
AND CLINICAL PRACTICE 

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ABSTRACT

The typical classification of prevention into primary, secondary, and tertiary categories has encountered various criticisms. We review the history and limitations of this and other classifications, and offer a substitute paradigm: five Stages of Prevention, which address consecutive steps in preventing acquisition and progression of diseases: 1) avoiding exposure to causative agents, 2) reducing acquisition of disease resulting from exposure, 3) interrupting advancement of acquired disease, 4) preventing complications from advanced disease, and 5) delay (or palliation) of death, or rehabilitation of disability, from complications. This new model can serve as a tool for health planning, including calculation of costs vs. benefits for investment of resources. It can also be applied to counseling patients on personal options for prevention.

CLASSIFYING PREVENTION: OVER HALF A CENTURY OF CHALLENGES

The complexity of prevention in the healthcare field makes a classification system theoretically useful. For any given disease or health problem, there may be a spectrum of opportunities for preventive interventions. Classification can help in a number of ways, e.g., to distinguish ranges or categories within that spectrum, in which interventions can be applied or should be developed.

Origins of the Three-Category Classification of Prevention and its Problems

The first use of the terms primary and secondary prevention may have been in a 1957 report (“Prevention of Chronic Disease,” volume 1 of an eventual 4) by the Commission on Chronic Illness, sponsored by the Commonwealth Fund. Primary prevention was defined as “averting the occurrence of disease,” secondary prevention as “halting the progression of disease from its early unrecognized stage to a more severe one and preventing complications” Health promotion, aimed at maintenance of health rather than prevention of diseases, was distinguished as type of prevention separate from primary prevention, which was considered to be “disease-oriented,” emphasizing the averting of occurrence of specific diseases (Harvard Univ. Press 1957, pp 1-68).

Leavell and Clark appear to be the first authors to have developed and gradually evolved a sophisticated classification system for prevention efforts. In 1953, in their “Textbook of Preventive Medicine,” (ref #) these authors described five levels of application of
preventive medicine: (a) health promotion, (b) specific protection, (c) early recognition and prompt treatment, (d) disability limitation, and (e) rehabilitation.

In the second edition of 1958, retitled “Preventive Medicine for the Doctor and His Community,” (ref #) Leavell and Clark classified and further defined the five levels into three categories: Primary prevention consisted of (a) health promotion (serving to further general health and well-being), and (b) specific protection (measures applicable to a particular disease or group of diseases in order to intercept the causes before they involve man). Secondary prevention consisted of (c) early recognition and prompt treatment (with the objectives of preventing spread to others if the disease is communicable, complications or sequelae, and prolonged disability). Tertiary prevention consisted of (d) disability limitation (prevention or delaying of the consequences of clinically advanced disease), and (e) rehabilitation (aiming at prevention of complete disability after anatomic and physiologic changes are stabilized). They did not at that time further conceptualize or define primary, secondary, and tertiary. Syphilis was used as an example to illustrate their concept.

In the Third Edition of their same text in 1965, Clark and Leavell referred to primary, secondary, and tertiary prevention as “phases” of prevention, incorporating among them the same five levels. However, disability limitation was transferred into the secondary category, leaving only rehabilitation as tertiary prevention.

Over the subsequent decades, a three-category paradigm of primary, secondary, and tertiary prevention, which we shall refer to as classical or traditional, has been adopted throughout many fields of medicine and the social sciences, e.g., cardiovascular diseases, respiratory diseases (Joseph et al., 2005), obstetrics (Decker & Sibai, Lancet Vol 357, 2001), infectious diseases (Liu, 2004), social sciences (Bloom, 1979), in addition to preventive medicine and public health. However, the definitions of the three categories has varied over time and from author to author.

Primary preventive efforts are generally considered to refer to measures aimed at preventing/reducing the risk of acquisition of disease or other unwanted health condition or state (Caplan, 1961, Gordon, 1983, Tannahill, 1985; Froom and Benbassat, 2001). However, most writers have not distinguished between avoidance of exposure to causative agents or factors, and mitigating the risks of acquiring disease due to such exposure. Most authors subsequent to Leavell and Clark have also omitted health promotion from primary prevention.

Secondary and tertiary prevention have been assigned variable meanings. They are generally understood as involving interventions at respectively earlier and later points when disease (or a precursor) already exists, however there is considerable variation among authors on where to divide line between the two (e.g., at the point of symptoms or of disability), and which types of interventions belong to each.

In 1961, Caplan defined secondary prevention (of mental illness) as reducing disease prevalence, through case finding and early treatment to decrease the duration of
established diseases (Caplan, 1961). U.S. Preventive Services Task Force (USPSTF) 1989 report (Guide to Preventive Services, Williams and Wilkins, p xxviii) defined secondary preventive measures as those that identify and treat “asymptomatic persons who have already developed risk factors or preclinical disease” but not clinically apparent disease, as opposed to primary prevention measures which were defined as those involving persons with neither symptoms nor risk factors or preclinical disease.

More recently, the Canadian Task Force on Preventive Health Care (1998) defined secondary prevention as aiming at detecting latent conditions and either reducing or halting their progression. On the other hand, Miller (1997) defined secondary prevention as reducing morbidity and mortality in patients with clinical disease manifestations, which overlaps with some definitions of tertiary prevention. In an atypical usage of the term. The Medical Letter (Vol 51, issues 1304, January 16, 2009) referred to prevention of recurrent cardiac arrest as secondary prevention,

[Add more tertiary definitions] The USPSTF 1989 report (Guide to Preventive Services, Williams and Wilkins, p xxviii) defined tertiary prevention as “preventive measures in symptomatic patients,” to prevent complications. In none of the above references was the concept of tertiary prevention utilized to address the prevention/delay of death, e.g., the reduction of disease-specific or complication-related mortality rates, or to increase quality or disability-adjusted life years.

Froom and Benbassat (2001) reviewed 317 abstracts utilizing the terms primary, secondary, and tertiary prevention, and noted a consensus in defining primary prevention as preventing a disease from occurring in the first place. However, they identified two main variations of the definitions of secondary and tertiary prevention, each adopted by reputable authors. In the “Leavell-Clark classification,” utilized by those authors and in two leading cardiology texts, secondary prevention was defined as “early diagnosis and prompt and adequate treatment to shorten the period of disability, arrest of the disease, prevention of complications and sequels, limitation of disability and prevention of death; tertiary prevention was limited to rehabilitation.” * On the other hand, in most textbooks of medicine and public health, they identified the “common classification,” in which all interventions in patients who are or have been symptomatic were included (along with rehabilitation) as tertiary rather than secondary prevention. They also noted that some abstracts identified attempts to prevent a complication of an established disease as primary prevention of the complication, while others considered similar interventions as secondary or tertiary prevention of the disease.

*Can’t find this in Leavell and Clark, and not grammatical; use 1965 Leavell and Clark 3rd edition, p. 24 instead.

Overall, Froom and Benbassat found inconsistent use of the terms primary, secondary, and tertiary prevention. They concluded that these three categories are not specific enough to be appropriately used.

Alternative Classification Proposals
Gordon in 1983 (Public Health Reports) proposed limiting the term “preventive” to measures practiced on persons who have not yet suffered any discomfort or disability due to the disease or condition in question. He then classified preventive measures according to their target populations: a) Universal measures, desirable for everyone; b) selective measures, targeted at above-risk demographics; c) indicated measures, targeted at individuals personally at risk due to risk factors or other abnormalities. While a potentially useful concept, this appears to us to be more of a classification for epidemiological selection of subjects for application of prevention measures, than a classification of prevention itself.

In 1985, Tannahill reviewed the usages up to that time of primary, secondary, and tertiary prevention by several authors, and found two different interpretation schemes, attributing one to Caplan (1961) and the other to Alderson, Fowler, and Barker and Rose (Tannahill, 1985). He found problems with both, including blurring at the interfaces he thought were arbitrarily introduced into a continuum of the natural history of diseases. He proposed the substitution of four foci for prevention: a) Prevention of the first occurrence of an illness or unwanted phenomenon; b) prevention of avoidable consequences of illness or other unwanted state through early detection when this favorably affects the outcome; c) prevention of avoidable complications of established disease or other unwanted state; and d) prevention of recurrence.

While this paradigm does consider both early and late foci for intervention, it does not separately distinguish the issues of exposure, progression, mortality, or disability. For most diseases, we believe that recurrence is more applicable to complications than to the underlying morbidity.

Froom and Benbassat proposed, as an alternative to the tripartite classification, an expansion of the categories of prevention from three to seven, which they found to correspond to the actual interventions utilized in the abstracts that they had analyzed. They subdivided primary prevention into Level 1, reducing exposure to an etiologic agent; and Level 2, increasing resistance to the disease. They left secondary prevention undivided as Level 3, defining it as screening for risk factors for disease (in asymptomatic individuals) in order to reduce them. Tertiary prevention was split into Level 4, prevention of recurrence (in asymptomatic individuals after a disease-related event); Level 5, treatment aimed at prevention of complications (in asymptomatic individuals after a disease-related event); Level 6, treatment of symptomatic patients for cure, palliation, or reduction of mortality; and Level 7, rehabilitation for “adjustment to irremediable conditions.” (F&B, 2001) They also recommended that clinical interventions be defined by their objectives, target populations, and types of preventive services.

While this proposed alternative classification is a creative contribution, and distinguishes additional types of interventions, it does not constitute a smooth and comprehensive continuum of prevention opportunities along the natural course of disease progression. It omits methods of preventing disease acquisition other than increasing resistance,
describes screening for risk factors but not for early disease, and omits delay of the progression of chronic disease, which have become the major causes of death in developed countries.

In the field of mental health, Cowan (1978) suggested reclassifying early secondary efforts as primary prevention, he and Bloom (1980) both arguing that action can only be taken after spotting early manifestation of problems. [Check Gordon, 1983, quoted in Sameroff chapter of Shaffer et al OSAP Monograph, 1990 as saying tripartite classification, epi research shows more complex causal models.] The Institute of Medicine (IOM) has since redefined prevention for the mental health field in terms of three categories, prevention (similar to primary prevention; this refers to interventions to ward off the initial onset of a mental disorder), treatment, and maintenance (IOM, 1994). In 2003, the Substance Abuse and Mental Health Services Administration adopted this IOM classification. (Ref)

However, although no one factor suffices as a cause, both risk and protective factors for the development of mental health disorders have been identified, residing within the individual, family, and community (Mental Health: A Report of the Surgeon General, 1999), (Sameroff, in OSAP Monograph 2). A new paradigm with additional components, such as exposure to such risk factors, applying protective factors to reduce acquisition, prevention of complications (e.g., suicidality, drug abuse or metabolic outcomes such as diabetes), and prevention of death from complications (e.g., by suicide, violence, or coronary events), might be more useful to mental health professionals than either the classical three categories or the IOM classification.

PROBLEMATIC ISSUES IN CLASSIFYING PREVENTION

Decreasing Relevance of Symptoms in an Age of Asymptomatic Chronic Disease

Many of the “common” usages of the terms secondary and tertiary prevention, as well as two of the three alternative classifications described above, refer in their criteria to the presence or absence of symptoms. However, major diseases of current public health importance such as HIV/AIDS, hepatitis C, coronary artery disease, hypertension, and diabetes can be asymptomatic for years as they stealthily progress and damage body organs; while other conditions like allergies and dermatitis may be immediately symptomatic without having progressed to serious morbidity. We therefore recommend increased recognition of asymptomatic disease. We further recommend limiting the reliance on symptomatology in the classification of disease states and of prevention to when symptoms are intrinsic to the definition of a stage of a specific disease. This is most relevant as an alternative to objective laboratory tests or imaging, in determining when a chronic condition has progressed to an advanced state that predisposes to complications, e.g., when coronary disease has progressed to the point of angina.

“Harm Reduction” and the Distinction Between Exposure and Acquisition
The controversial concept of “harm reduction” surfaced during the 1990s in relation to reducing risks for drug addicts (DeJarlais, DiClemente, Marlatt, Rocky Mountain Center for Health Education and Promotion, 2001; Leshner (2008). Definitions on the Web and literature vary, but generally refer to reducing the negative consequences of drug abuse and other high-risk behaviors (e.g., sexual), in persons who will not discontinue those behaviors. Some “harm reduction” interventions such as needle exchange can lay claim to being primary in that they aim to reduce disease incidence. However, such strategies do not emphasize avoidance of exposure to the causes of disease (Rocky Mountain Center).

Avoiding exposure to the causes of disease should be considered as more “primary” than continuing such exposure and attempting to mitigate its adverse effects, however the latter is an essential backup whenever exposure cannot be eliminated. Since no method of mitigating the risks of exposure is 100% effective, “harm reduction” cannot be as effective as complete abstinence from the causes of disease. Dependence solely on “harm reduction” strategies is especially risky when only a few exposures to a dangerous behavior (e.g., needle sharing) can result in life-threatening disease. The “harm reduction” concept can most usefully be applied as part of a larger spectrum of prevention, in which abstinence from the causative agents of disease is always the optimal plan for disease prevention but cannot always be achieved, and disease acquisition typically requires multiple exposures.

By not distinguishing exposure avoidance from mitigating the disease-acquisition effects of exposure, the classical paradigm has limited usefulness for counseling individual patients on their options within the spectrum of prevention. A new paradigm, assigning exposure avoidance and reduction of disease acquisition despite exposure to two strategies to different stages of prevention, could be helpful in clarifying such options, e.g., sexual abstinence vs. condom use; avoiding drug abuse vs. using clean needles.

**THE STAGES OF PREVENTION**

We propose a new paradigm, which we shall refer to as the Stages of Prevention, that we believe helps to resolve many of the above shortcomings of the traditional model and previous alternatives of the last half century, and offers corresponding advantages. The term “stages” is proposed to note the tendency of many diseases, particularly those that are chronic, to progress over time. To introduce and explain the new model, we shall first review the logical stages of acquisition and progression of chronic diseases. For self-limited diseases without progressive courses and longterm complications, some but not all stages of the paradigm may be applicable.

1. Exposure to the agents or causes of disease.
2. Acquisition of the disease condition as a result of this exposure, at an early stage (which is generally free of morbidity, but for some infectious conditions may already be contagious to others).
3. Advancement/progression of the disease process that has been acquired, to the causation of clinically significant illness.
5. Death or disability due to the complications.

We propose that there is a stage of preventive intervention that corresponds to each major stage in the spectrum of development of disease. In applying these stages, we agree with Froom and Benbassat (2001) on the great importance of specificity in defining the condition that is to be prevented, and in being as specific as possible in defining the details of the preventive intervention. Without such specificity, no classification system involving progressive levels or stages will easily avert confusion.

Table 1. Stages of Disease Development and Corresponding Stages of Prevention

<table>
<thead>
<tr>
<th>Stages of Disease Development</th>
<th>Corresponding Stages of Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Exposure</td>
<td>Avoidance of Exposure</td>
</tr>
<tr>
<td>2 Acquisition</td>
<td>Reduction of Acquisition</td>
</tr>
<tr>
<td>3 Advancement/Progression</td>
<td>Interruption of Progression</td>
</tr>
<tr>
<td>4 Complications</td>
<td>Avoidance of Complications</td>
</tr>
<tr>
<td>5 Death or Disability</td>
<td>a) Delay of Mortality</td>
</tr>
<tr>
<td></td>
<td>b) Rehabilitation of Disability</td>
</tr>
<tr>
<td></td>
<td>c) Palliative Care for Inevitable Death</td>
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**Stage 1: Exposure avoidance**

If this type of prevention, which we shall call Stage 1, can be achieved, it is generally the safest option and can sometimes be the least expensive on a per capita basis. On the other hand, it may need to be applied to an entire at-risk population rather than to persons who have been exposed, increasing the total costs in comparison with Stage 2 measures. Examples: abstinence from smoking, drug abuse or unsafe sex, avoidance of unsafe locations or machinery; restricting trans-fats. Screening of potential disease sources can play an important role; e.g., unprotected sex between two monogamous partners who have tested negative for HIV on two occasions 6 months apart is extremely unlikely to represent HIV exposure. The same activity that constitutes an exposure if a disease risk is present may not constitute an exposure if disease risk is absent. Screening for risk factors that constitute exposure (rather than markers of early disease) also falls under Stage 1 prevention, e.g., testing a home for lead or radon, or taking a dietary history for foods which could lead to the risk of heart disease.

Although total abstinence from exposure is theoretically the only 100% effective way of avoid disease, an intervention for avoidance does not have to be 100% effective to be classified in this stage. For example, a 20% reduction in exposure may reduce disease acquisition by a like percentage, which would be an impressive accomplishment. With an infectious disease, achieving reduced shedding or propagation from the source counts as exposure avoidance, e.g.,
isolation of a tuberculosis patient. Immunization may be a means of exposure avoidance if it suppresses the prevalence of the disease.

Exposure must be clearly defined, and the population at risk of exposure must also be described in order to determine the exposure rate and the target group for intervention. Will exposure to sexual risk of HIV be defined as anyone in the population who is sexually active, having unprotected or non-monogamous sex, or having a sexual partner who is HIV positive? The disease to which the exposure contributes must also be clearly defined.

Often, disease results from behavior, but the behavior may be defined either as exposure or as acquired disease. Thus, smoking, drug abuse, or alcoholism may be defined in some studies as the disease condition, with exposure consisting of the factors that contribute to such behaviors, such as attitudes and perceptions of risk (Song, Morrell, APHA March 2009). On the other hand, if the disease in a study is defined as lung cancer, smoking can be defined as an exposure, and similarly alcohol consumption as exposure to cirrhosis risk, and injection drug use as exposure to hepatitis C. This can lead to variations in usage from one study to another, similar to those found for the three-level classification (Froom and Benbassat), but we do not consider this as a weakness of either paradigm, since both are dependent on the definitions selected for any particular case. The Stages of Prevention paradigm can function effectively for any health condition in question, once it and related variables have been clearly defined.

An important caveat is that exposure avoidance, if excessive, can actually be harmful to personal or public health. Avoidance of injury by staying at home and not exercising can predispose to obesity, diabetes, and heart disease; avoidance of infection by eschewing social interaction can be socially and emotionally crippling. Permanent sexual abstinence could deny a person the benefits of loving sexual relationships, marriage, and parenthood; therefore abstinence is generally thought of as a temporary recommendation (e.g., during the teen years, or until marriage, after which sexual activity may be presumed to be less risky). Also, the welfare of the community depends on a sufficient number of citizens taking the risks involved in such tasks as police, firefighting, and disaster response work. Thus, it is helpful if exposure can be defined in such a way that it implies excessive, unnecessary, and particularly hazardous vulnerability.

Epidemiologists are trained to think in terms of risk factors for disease, but while some things treated as risk factors may be causative factors for which exposure avoidance is relevant, others may simply be markers for disease, or may even be caused by early disease. Future epidemiological research should place increased emphasis on distinguishing among these, so that we can avoid only those risk factors that truly contribute to the development of disease.

**Stage 2: Prevention of acquisition as a result of exposure**
Acquisition means acquiring a disease agent such as an infectious organism, or acquiring an early (and usually asymptomatic) form of a disease. This stage does not reduce exposure but reduces the chance of disease whenever exposure occurs. If Stage 2 prevention can be achieved, it is generally the next safest option after Stage 1, and may often be the least or second least expensive. If process indicators are utilized, Stage 2 prevention can be measured by the rates of distribution and use of interventions such as condoms or infant care seats. However, outcome indicators for Stage 2 prevention are more important, and consist of rates of disease acquisition as determined by surveillance among the population groups exposed to risk of the disease. Stage 2 prevention can never be completely effective, because exposure persists, and no method of mitigation of acquisition of disease from exposure is totally effective.

Examples: Using condoms but having sex when it is not known that two partners are both monogamous and uninfected; restricting the number of sexual partners; taking malaria prophylaxis when entering malarious areas; using clean needles but continuing injection drug use; utilizing seat belts and shoulder harnesses to reduce the risk of automobile accident fatality despite continuing to drive in the same vehicles and on the same roads. Note that immunization can fall into this stage, when it does not reduce exposure to the cause of disease but is used to reduce the risk of acquiring the disease from exposure, e.g., providing rabies vaccine to veterinarians who continue to handle potentially rabid animals; and annual influenza vaccine campaigns, which are not expected to avoid exposure to influenza during outbreaks but rather to reduce the chances of acquiring influenza from such exposure.

Some interventions that utilize Stage 2 of prevention are components of the agenda proposed by advocates of “harm reduction,” e.g., needle exchange to help avoid bloodborne pathogens despite the continuation of drug abuse, and condoms to avoid infection or unwanted pregnancy despite the continuation of sexual activity.

Increasingly, genetic predispositions can be determined by screening and may be considered as exposures that may be unavoidable, suggesting the need for targeted Stage 2 interventions for those genetically at risk. Table 2 includes such targeted Stage 2 efforts for breast cancer, for women with the BCRA gene. Boardman (JPHA March 2009) recently reported that up to 50% of daily smoking (though not smoking onset age) is genetically influenced (presumably due to differences in nicotine metabolism), but can be influenced by marketing restrictions and taxes.

Perhaps the most critical requirement for any Stage 2 strategy is to clearly define what is meant by the disease or condition in question (as already noted in the discussion of substance use in the section on Stage 1, above). For diabetes, will the criteria for prediabetes or full-blown diabetes be used? If the former,
Stage 3 could be avoidance of progression to full-blown diabetes; if the latter, advanced diabetes would have to be defined with respect to Stage 3. In the early days of HIV/AIDS, AIDS was defined as the disease; now HIV infection manifested by a positive antibody test is the usual criterion. Since the rate of acquisition of disease has as its denominator the population exposed, this rate is equally dependent on clear definitions of exposure and of the population at risk, as discussed under Stage 1.

**Stage 3: Interrupting/delaying the advancement of acquired disease**

This roughly corresponds to the classical concept of secondary prevention, and implies the ability to detect early disease and to intervene to slow or even prevent its progression. Thus, screening of populations at risk for disease falls into this stage, if it is capable of detecting early disease and is followed up by intervention to prevent progression to a more serious state. If process indicators are utilized, Stage 3 can be measured in terms of rates of screenings done, early cases detected, and/or early treatment initiated. However, outcome indicators for Stage 3 prevention are more valuable, and consist of measurement of reduction in cases meeting the selected criteria for advanced disease.

Application of a Stage 3 prevention strategy requires a clear definition of advanced disease, as has been done for AIDS as an advanced stage of HIV. Advancement of disease can also be subdivided, with definitions of progression of a disease through various progressive stages (which in the prevention paradigm would be substages), as have been defined for various cancers and congestive heart failure (American College of Cardiology, ACC & McCormick, 2007-8). The rate of progression per cases of early acquired disease depends upon the previously discussed definitions for the disease, its acquisition, exposure, and the target population.

Those “harm reduction” methodologies in which a disease state such as addiction has already developed, but has not progressed, fall into this stage of prevention, e.g., detecting drug or alcohol abuse or smoking, and then providing effective treatment such as methadone that does not cure addiction but helps to prevent complications of more dangerous narcotics obtained for street sources. Other examples: detecting pre-diabetes (if it is defined as a disease or health condition) or early diabetes, then instituting effective glycemic control and reducing insulin resistance to retard macrovascular and microvascular changes; detecting elevated cholesterol, then treating it to avoid the progression of atherosclerosis; screening for HIV, then prescribing antiretroviral drugs at an appropriate time to delay the onset of AIDS; detecting cervical dysplasia through Pap testing, and then effectively treating it to prevent cervical cancer. The zoster vaccine might be considered to be a Stage 3 intervention, in that it helps prevent the progression of latent herpes zoster to symptomatic shingles (unless the latter is considered as a complication, in which case the vaccine serves a Stage 4 purpose).
When addictive behavior is defined as a disease condition, prevention of relapse of the behavior can be considered to be within this stage. Prevention of recurrent loss of control that may worsen any physical disease similarly fall into Stage 3, e.g., exacerbations of diabetes, or recurrences of uncontrolled hypertension. If a relapse can lead to a complication, prevention may be Stage 4; if it is likely to be fatal, prevention may be Stage 5, or it can be proportionally attributed to Stages 4 and 5. In this, we do not concur with making relapse prevention a separate stage as proposed by Tanahil (1985) and by Froom and Benbasset (2000).

**Stage 4: Averting/delaying serious complications of advanced disease**

[Insert definitions of complications with references] Once advanced disease has already developed, additional preventive measures, which we classify as Stage 4, are often available and necessary to avert or delay the incidence of complications. Examples: Use of anticoagulants for persons who already have advanced heart disease; performance of vascular surgery to avert myocardial infarction or stroke; treatment of cancer that has already spread to avoid life-threatening metastases; performance of liver transplants for hepatitis C patients with end-stage liver diseases.

Because of the body’s weakened state, Stage 4 prevention is sometimes less effective than the previous stages; may also be much more expensive. However, there are some relatively inexpensive measures that fall into this category, such as the prescription of aspirin to help avoid thrombotic events in persons who already have coronary or cerebral atherosclerosis, or of trimethoprim-sulfamethoxazole to prevent *Pneumocystis* and bacterial pneumonias, as well as the activation of latent toxoplasmosis, among persons with AIDS. The restriction of treatment in Stage 4 to persons who already have advanced diseases, rather than to entire community populations, is a significant source of cost-saving.

Complications may tend to recur, such as repeated myocardial infarctions or bouts of opportunistic infections. Therefore, Stage 4 prevention may need to be ongoing to prevent recurrences. Prevention of recurrent heart attacks or strokes still falls under Stage 4.

Each disease may have several identified complications; a preventive intervention may be targeted at one or several of these, e.g., renal failure, blindness, and cardiovascular disease in advanced diabetes. If prevention of all major complications of a disease is being considered, and if strategies vary for different complications, Stage 4 must be divided into subunits to be separately calculated and then combined.
Each complication and its diagnostic criteria should be clearly defined. The rates of each complication depend also on the previously discussed definitions of advanced disease or categories of progression, and the population at risk for the complication.

**Stage 5: Delaying/reducing the risk of death or chronic disability from serious complications**

Once a serious complication of disease has already occurred, it may have a potential to cause death that is preventable, may cause some degree of disability that is subject to rehabilitation, or may lead to a terminal condition for which palliation can be applied. We have therefore offered three alternative types of interventions for this stage. Stage 5a is prevention (significant delay) of death, Stage 5b is rehabilitation for disability, and Stage 5c is palliative/end of life care. Stages 5a and 5b may be combined in the care of a given individual.

On the other hand, some measures that avert death can be highly cost-effective, including at least one “harm reduction” technique, i.e., providing syringes with naloxone to household members to revive addicts in the event of discovery of potentially lethal overdose. Other interventions may be more intensive but still cost-effective, e.g., administering prompt thrombolytic therapy after acute myocardial infarction or stroke, or applying advanced cardiac life support for cardiopulmonary arrest.

Sometimes the continuation of Stage 3 or 4 interventions may have a significant effect on mortality reduction. For example, the mortality rate among HIV-infected patients being treated for tuberculosis in Thailand was found to be reduced by 84% if antiretroviral therapy (ordinarily used to control HIV progression) was concurrently administered (Aakslip et al, EID, 2007).

Calculation of the mortality rate of a specific complication is of course dependent on the definition of that complication, and the ability to estimate the population suffering from it. All of the previously discussed definitions and criteria apply.

Rehabilitation for a complication that can resolve and in which function can improve can be considered restorative rather than preventive, however it also can be considered as preventive of chronic disability. Even when chronic disability has already developed and cannot be reversed, we have accepted the value of rehabilitation in preventing further deterioration, averting recurrence, and reducing dependence.

Although our only listing of rehabilitation is in Stage 5b, rehabilitative interventions can have preventive value in the traditional sense at other levels of prevention. Thus, physical therapy after a stroke may increase mobility and help to prevent an additional complication of deep vein thrombosis (Stage 4...
prevention), or when used for obesity may slow progression of the condition (Stage 3 prevention); while drug abuse rehabilitation may help to prevent HIV or viral hepatitis either by substituting methadone for injections (Stage 2 prevention for those diseases), or by preventing further abuse of drugs altogether (Stage 1 prevention for HIV or viral hepatitis, or for drug abuse itself).

When applied to individuals who are terminal or have poor prognoses, treatment to delay death, such as liver transplants to patients with terminal liver disease, and administering renal hemodialysis or renal transplants to patients with renal failure, may be the most expensive and least cost-effective type of prevention. After some consideration, we have recognized that palliative care such as hospice deserves a place in the pantheon of prevention, because it can prevent pain and other discomfort, as well as needless expense for futile treatment.

Since ultimately everyone dies, all reductions in mortality rates constitute delay rather than total avoidance of death. Palliative care may not even delay death but may improve the quality of remaining life, as may rehabilitation for chronic disability. Therefore, the effectiveness of Stage 5 prevention should be measured not only in terms of reduction of death as a short-term consequence of a particular disease complication, but also in terms of life years. The widely used indicator QALY (quality-adjusted life years) can measure the combined effects of Stage 4 and 5 prevention. [Insert Ref and formula for calculation]

Multi-stage Preventive Measures

Froom and Benbassat (2000) noted that some medical interventions elude classification because they may have effects at more than one level. Health education is an example, because unless the messages provided are extremely specific, education can help in avoiding exposure to disease, encouraging measures to mitigate the effects of exposure, encouraging screening for early disease and entry into the healthcare system for treatment, prevention of complications, and survival in the event of complications. We suggest that the preventive effects anticipated from such measures be allocated into the stages of prevention they are expected to affect, with a proportion ascribed to each stage.

Prevention of Transmission of Communicable Diseases: Double Credit

Detection and early antimicrobial treatment of many communicable diseases constitutes Stage 3 prevention for the persons already infected, but generally also results in reduced shedding of the infectious organism, and so also serves as Stage 1 prevention for persons who would otherwise have been exposed. For a chronic communicable disease such as HIV/AIDS, antiretroviral treatment generally continues indefinitely, and even after the disease is advanced helps to avoid complications (Stage 4). Some other measures applied to persons infected with communicable diseases, strictly for public health and infection control, do not interrupt the course of the disease and can be considered strictly as Stage 1 prevention for the potentially exposed uninfected.
APPLICATION OF THE STAGES OF PREVENTION TO SELECTED DISEASES

The followings are three examples of how our paradigm could be applied to three specific diseases. This type of classification could be helpful in the field of health planning, to lay out all the options and then consider the cost-effectiveness of investing in interventions at each level. It could also be valuable in the counseling and treatment of individuals in a clinical practice, giving patients their range of options for prevention, particularly emphasizing the choices between stages 1 and 2 for those who do not yet have a disease in question, and between stages 3 and 4 for those who have already acquired it. The assignment of specific interventions to the various stages could be debated based on different definitions and criteria for the disease states and complications. One of these diseases, HIV/AIDS, will also be discussed under applications to health planning.

Table 2. Application of Stages of Prevention Paradigm to Three Selected Diseases

<table>
<thead>
<tr>
<th>Stages</th>
<th>Disease I</th>
<th>Disease II</th>
<th>Disease III</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Exposure Avoidance:</td>
<td>Healthy eating, limit simple carbohydrates, maintain healthy weight, exercise</td>
<td>Abstinence from sex (or screening and monogamy of seronegative partners), no injection drug use</td>
</tr>
<tr>
<td>2</td>
<td>Disease Acquisition Reduction:</td>
<td>Weight loss, consider metformin if insulin resistance/pre-diabetes</td>
<td>Condom promotion and programs to discourage drug abuse, needle sharing</td>
</tr>
<tr>
<td>3</td>
<td>Interruption or Delay of Disease Advancement:</td>
<td>Anti-diabetic drugs, monitor hgb A-1C, FBS, proteinuria, lipids; bariatric surgery if indicated</td>
<td>Antibody screening, monitoring CD4, viral load; treatment with antiretrovirals</td>
</tr>
<tr>
<td>4</td>
<td>Avoidance or Delay of Disease Complications:</td>
<td>ACE Inhibitor/ARB to prevent renal sequelae, strict glucose control (insulin if necessary), lipid control, foot and eye care</td>
<td>Prophylactic treatment for opportunistic infections</td>
</tr>
<tr>
<td>5a</td>
<td>Delay of Mortality from Disease:</td>
<td>Renal Dialysis, coronary stent or bypass</td>
<td>Intensive treatment for severe opportunistic</td>
</tr>
</tbody>
</table>
Use of the Stages of Prevention in Counseling Individual Patients

The three-category paradigm has limitations for use in discussing prevention options with individual patients. Patients can be educated on the concept of primary prevention to avoid getting a disease (e.g., immunization); of screening as secondary prevention to pick up early disease (e.g., getting Pap tests or colon cancer screening); and of tertiary prevention to prevent worsening of existing disease (e.g., staying on blood pressure or diabetes medication). However, the Stages of Prevention model includes more steps corresponding to personal behavioral decisions and health strategies and could be more helpful in counseling individual patients and groups on their personal options within the spectrum of prevention. This applies especially to discussion with patients about avoiding exposure as distinguished from continuing exposure-prone behavior and attempting to reduce its harmful potentials. It can also help in counseling patients with chronic diseases on the measures that can be taken to retard disease progression, prevent the complications that are more likely with advanced disease, and prolong life or deal with disability if complications arise.

There will always be tradeoffs where exposure is concerned, and some individuals will choose to risk the exposure and depend more for protection on the mitigating measures of Stage 2. We think that the general public, including patients in clinical practice, should be educated on the risks of common hazardous exposures, and presented with choices of categories and interventions to apply to their personal lives. The new paradigm presents disease as a multi-stage continuum, in which preventive treatment at the earliest stage possible is most effective. This is a concept that can be communicated to patients to assist in counseling.

Mathematical Uses and Applications in Health Planning

The classical three categories of prevention have not often been linked in a mathematical manner, to facilitate the calculation of cost-effectiveness of interventions at each successive step or stage in the spectrum of acquisition and progression of disease. Although this can be done, there are not enough steps in the three-level paradigm to track and interrelate the rates of preventable stages of diseases from exposure all the way through mortality.

As each stage of prevention is applied, it can reduce the rate of its respective stage of disease development. If the effectiveness of any given preventive measure is known and the respective stage of disease development to which it is applied is reduced accordingly, the rates of disease, complications, and death can consequently be reduced in a mathematically calculable manner. The new rates, calculated by multiplying the reduced rates together, can be subtracted from the old to determine the net rate reduction.

Estimates of potential effectiveness also should be based on evidence-based research that has been specific with respect to the above.
As the rates related to each of these stages are cumulatively multiplied together as factors, the products represent the probability, per total population at risk, per time period (usually utilizing a year), of the last factor having been achieved. Thus, the rate of disease acquisition is equal to the rate of exposure multiplied by the rate of disease acquisition per exposure (or per thousand or hundred thousand exposures). The rate of progressing to advanced disease is in turn equal to the rate of disease acquisition multiplied by the rate of disease advancement/progression per acquired disease. The rate of developing a complication is equal to the rate of advanced disease multiplied by the rate of the complication per case of advanced disease (or per thousand or hundred thousand cases).

Ultimately, the death rate in a defined population p per year or other time period t, due to complication-specific mortality, $D/(p^*t)$, is equal to the product of five factors: the exposures per defined population per year, $E/(p^*t)$, the rate of disease acquisition per exposed persons ($A/E$), the progression rate of acquired disease per acquired cases ($P/A$), the rate of complications per cases of progressed disease ($C/P$), and the complication-specific death rate ($D/C$).

$$D/(p^*t) = E/(p^*t) * A/E * P/A * C/P * D/C$$

If the rate of an earlier stage is needed, it will be the product of the rates of the stages up to that point, e.g. the rate of a specific complication within the defined population is equal to $E/(p^*t) * A/E * P/A * C/P$, and the incidence rate of the disease is equal to $E/(p^*t) * A/E$.

After applying the expected reductions in rates from preventive interventions, the reduced rates can be calculated, and the reduction in cases compared with the associated costs. If the baseline rates for each stage of disease development are represented as $B_1$ through $B_5$ respectively, and the rate reductions achievable for interventions at each stage are represented by $R_1$ through $R_5$ respectively, the potential rate of reduction of a specific complication ($R_c$), resulting from a program combining exposure reduction, acquisition reduction, prevention of disease advancement, and avoidance of the complication would be:

$$R_c = B_1 * B_2 * B_3 * B_4 * (1-R_1) * (1-R_2) * (1-R_3) * (1-R_4)$$

The equations become more complicated if separate exposure rates to different causative factors for the disease, and separate complication rates for different complications, are included.

Utilized in this manner, our stages of prevention can be a useful tool for planning by policy makers for public health agencies or healthcare delivery systems, in applying resources to prevent illness in target populations.

**Further Consideration of the Example of HIV/AIDS**
For the prevention paradigm to work effectively, it is important to define a specific disease condition and the criteria for disease advancement. In the case of HIV/AIDS, in the 1980s the disease was defined as AIDS, but today a positive HIV test defines early disease and AIDS is considered a late manifestation. With this infectious disease, Stage I, Exposure Avoidance, is generally understood to include abstinence from sex, and avoiding injection drug use that may involve needle sharing. However, depending on definitions selected for exposure, persons engaging in sexual activity with a partner who has tested negative for HIV, or in injection drug use without needle sharing, could be considered as practicing either Stage 1 or Stage 2 prevention.

Stage 1 intervention through education in a low prevalence population is reported to be cost effective, but individually focused intervention is more cost effective in a higher prevalent population (Cohen DA et al., 2004). Stage 2 prevention through condom use can reduce HIV acquisition by 90% from ongoing sexual encounters, and a 10% reduction in HIV acquisition among injection drug users can be achieved through provision of clean needles at pharmacies (Cohen DA et al., 2004). A state-wide study done on cost-effectiveness of a condom distribution program in Louisiana in 2001 reported the cost of approximately $2 per person per year prevented between 94 and 156 HIV infections, saving between $18 million and $30 million in medical costs. It is noted that the condom distribution program also had significant effect on reducing ‘at risk’ behavior (Cohen DA et al., 2004).

Stage III intervention is specifically to delay or interrupt disease progression. For those who are already HIV infected, the interventions aim to delay progression to AIDS by first screening the high-risk population with a standard or rapid HIV test. For those testing positive, studies have shown that early detection and antiretroviral treatment delay progression to AIDS by 10 to 20 years [Reference]. Once a diagnosis of AIDS has been made, Stage 4 intervention will delay further disease progression/deterioration. An example is provision of trimethoprim-sulfamethoxazole in AIDS patients with CD4 count less than 200 to prevent PCP pneumonia. With decreasing CD4 numbers, severe opportunistic infections become more common. Stage V would involve reduction in mortality by prompt treatment of life-threatening opportunistic infections. An average cost of one-day stay in ICU is $1500 (Dasta et al., 2005; Noseworthy et al., 1996; Norris et al., 1995) and patients with severe life threatening infections will most likely stay a few days as oppose to a regular floor bed will cost less than half as much. Although cost effectiveness varies among interventions, intensive hospital-based treatment of advanced complications will generally be much more expensive than early treatment to prevent the complications.

**A CONVERSE PARADIGM, BEYOND DISEASE PREVENTION: THE STAGES OF HEALTH PROMOTION/WELLNESS**

The classification presented in this article applies to diseases, and other adverse health conditions such as injuries, caused by exposures to hazardous agents or factors. Each of our prevention stages has been presented as an intervention in a chain of negative events. We have not included health promotion in any of these stages, however it is noteworthy
that for the pioneers Leavell and Clark, it was the first level of prevention, whereas the Commission on Chronic Illness considered it to be a separate category from primary and secondary prevention.

Breslow (JAMA 1999, March 17 1999 281(11) 1030-1033, From Disease Prevention to Health Promotion) cited a 1985 World Health Organization formulation that health is “physical, mental, and social well-being, not merely the absence of disease and infirmity,” and proposed in 1999 moving “beyond disease prevention, i.e., the effort to avoid or minimize pathological conditions,” and aiming for “the energy and reserves of health that permit a buoyant life, full of zest the eager ability to meet life’s challenges.” Health promotion and wellness can thus be considered in a more positive sense.

A supplementary paradigm including four stages of health promotion/wellness could be utilized to classify such efforts. Stage 1 would be exposure to positive health influences. Stage 2 would be adoption of positive health practices (such as healthy diet, exercise, recreation, adequate sleep, etc.). Stage 3 could be an increase in indicators of health and wellness due to the healthy practices (such as increased strength and flexibility, immunity, optimal BMI, etc.). A Stage 4 involving the achievement of specific defined health and wellness goals, both subjective (e.g., sense of wellbeing and energy, fulfilling social relationships), and objective measures (e.g., high cognitive function, productivity, capacity for role fulfillment or achievement). Such a model is beyond the scope of this article, but deserves consideration in future studies.

CONCLUSIONS

We have presented a proposal for a new classification of prevention services and interventions, consisting of five stages, each directed toward preventing a successive state in the development and progression of disease, i.e., exposure, disease acquisition, disease progression, development of complications, and death or chronic disability. We recommend that the new five-stage classification be utilized as the new paradigm for understanding and applying prevention in public health and in healthcare practice. We also recommend that future studies and public health programs apply this model, and that if it proves as useful as we expect, that it ultimately replace the old classification of primary, secondary, and tertiary prevention, which as we have shown has serious limitations for use in today’s healthcare environment.

The Stages of Prevention paradigm is most valuable with respect to diseases or other health conditions such as trauma, that result from exposure to causative factors, and which tend to progress to advanced stages with risks of complications and death. Thus, all five stages can be readily applied to the diseases that are the major causes of death in the United States, cardiovascular, neoplastic, metabolic, and serious infectious diseases (CDD, National Center for Health Statistics), and to chronic diseases in general. For mild and self-limited diseases, not all of the five stages may be relevant, but the paradigm can still be useful for those that are. Clear definitions of disease exposure and of the exposed population, disease acquisition, progression, complications, and interventions must be developed for optimal usefulness of new classification.
Using the paradigm, a concrete plan of intervention can be developed at various stages where public health policy development, research, or clinical settings with individuals or groups to provide the best prevention options. When used for public health and health systems planning, interventions at several stages can be combined and their benefits and costs calculated. In clinical practice, the paradigm can be used in laying out the options available to a patient for prevention, and for helping the patient to select the most appropriate and acceptable interventions.

About the Authors

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