The 5 Stages of Disease and Prevention

A New Classification System Based on How Diseases Actually Develop and Can Be Prevented

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Previous versions posted at Academia.edu, Researchgate.net, and Capreventivemed.org.

References at end.

Objectives: Participants should be able to:

- Understand the history of the traditional classification of prevention efforts into "primary, secondary, and tertiary," and its criticisms and limitations
- Discuss advantages and limitations of a new 5-stage classification system, based on prevention of 5 corresponding stages in the development of diseases
- Classify various types of preventive interventions, using at least one classification system
- Describe how to utilize at least one classification paradigm in health planning and patient counseling

Basic questions about prevention

- How would you define prevention and Preventive Medicine?
  - What are the elements? The "nuts and bolts"?
- What are the steps/stages through which chronic and slowly-developing diseases and other medical conditions develop?
- What can be done at each stage to stop or slow the process?
- Is there a role for prevention in every medical specialty, at every stage of disease?

Classifying Prevention: Six Decades of Challenges

- Classification can help in a number of ways
  - Break down and define what we mean by prevention
  - Guide thinking and planning for prevention by selecting categories within that spectrum
  - Select which interventions can be applied or should be developed for particular diseases and stages of disease
  - Compare costs and benefits of interventions at different points in the classification system
- **For any given disease or health problem, a spectrum of opportunities for preventive interventions exists**

Origins of the Primary/Secondary/Tertiary Classification of Prevention: Leavell and Clark

- Hugh Leavell (Harvard SPH) and E. Guerney Clark (Columbia SPH): first authors to develop and gradually evolve a classification system
- In 1953, their Textbook of Preventive Medicine described **five levels** of application of preventive medicine:
  - (a) health promotion
  - (b) specific protection
  - (c) early recognition and prompt treatment
  - (d) disability limitation
  - (e) rehabilitation.

Origins of the Three-Category Classification of Prevention

- 1st known use of terms primary and secondary prevention: 1957 report, Prevention of Chronic Disease
  - *Commission on Chronic Illness, sponsored by Commonwealth Fund, Harvard Univ. Press 1957, volume 1*
  - - Primary prevention: "**averting the occurrence** of disease"
  - - Secondary prevention: "**halting the progression** of disease from its early unrecognized stage to a more severe one and **preventing complications**"
  - - Health promotion was considered differently: aimed at maintenance of health rather than prevention of diseases
    - A type of prevention separate from primary, which was considered to be "disease-oriented"

Origins of the Three-Category Classification of Prevention, Leavell and Clark, contd.

- First classification into 3 categories, further defined:
  - In 2nd edition, 1958 (1 year after the chronic disease report which introduced primary and secondary prevention), retitled "Preventive Medicine for the Doctor and His Community":
  - Primary prevention (1st 2 components of 1953 classification):
    - (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)

Origins of the Three-Category Classification of Prevention, Leavell and Clark, contd.

- Secondary prevention (3rd component from 1953):
  - (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 (new, not included in the chronic disease report; 4th and 5th components from 1953):
  - (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)

Origins of the Three-Category Classification of Prevention, Leavell and Clark, contd.

- In 3rd edition of same text (Preventive Medicine for the Doctor and his Community), 1965, Leavell and Clark referred to primary, secondary, and tertiary prevention as "phases" of prevention
  - - Same five components (a) through (e) in last 2 slides distributed among them
  - - Disability limitation was transferred to secondary category, leaving only rehabilitation as tertiary prevention.

Origins of the Three-Category Classification of Prevention, contd.

- Since mid-1960s, three-category paradigm of primary, secondary, and tertiary prevention has been adopted in many fields of medicine and social sciences, in addition to Preventive Medicine and public health
  - However, definitions of the three categories have varied over time and from author to author
- In medical literature, primary prevention generally refers to preventing or reducing risk of acquiring disease (or other unwanted health condition) before it has developed
  - But in the social sciences, Bloom (1980, J. Prevention) found multiple definitions and usages of the term from 1960's to then

Origins of the Three-Category Classification of Prevention, contd.

- Where does health promotion fit?
  - The place of **health promotion** has been variable
    - Leavell and Clark included as primary prevention in all 3 editions, but in 1965 said not widely utilized, and not applied for specific diseases
    - Most subsequent authors omitted from classification
    - Lifestyle components such as avoiding risks and healthy diet fit into most conceptions of primary prevention
    - To be dealt with further, later in this presentation

Origins of the Three-Category Classification of Prevention, contd. (my critique)

- Concept of primary prevention fails to distinguish between preventing exposure, vs. mitigating disease risks resulting from exposure, e.g., "harm reduction"
  - "Harm reduction" generally refers to reducing negative consequences of drug abuse and other high-risk behaviors (e.g., sexual), in persons who will not discontinue those behaviors
    - - Origin of theory: Rotterdam, 1980s (Springer E, Focus, January 2004)
    - Prime example: needle exchange for injection drug users
  - Most "harm reduction" interventions are considered primary prevention in that they aim to reduce disease incidence
    - - An essential backup whenever exposure cannot be eliminated
- Avoiding exposure to the causes of disease, when possible, can be considered more "primary" (and more effective, if actually accomplished) than continuing such exposure and attempting to mitigate risk of acquiring the disease

Origins of the Three-Category Classification of Prevention, contd.

- Secondary prevention has been assigned variable meanings:
  - Leavell and Clark (1965): "**early diagnosis** and prompt treatment" to:
    - Prevent spread to others if disease is communicable
    - **Cure or arrest the disease process to prevent complications** or sequelae
    - Prevent prolonged disability
  - Miller (1997): prevent further morbidity and reducing mortality in patients with **clinical manifestations** of disease
  - USPSTF (1989) in contrast reviewed only **asymptomatic** patients for both primary and secondary prevention

Origins of the Three-Category Classification of Prevention, contd.

- Screening for early disease is commonly thought of in connection with secondary prevention
  - - Note that **screening by itself detects but does not prevent disease**
  - **- Follow-up interventions needed to constitute prevention**
- Secondary Prevention: different uses of term
  - - Medical Letter (and scattered in literature): avoiding **second occurrences of disease episodes** like cardiac arrest
  - - Communicable diseases: prevention of **secondary cases**

Origins of the Three-Category Classification of Prevention, contd.

- Tertiary prevention likewise is variably defined:
  - Leavell and Clark (1965): only **rehabilitation**
  - Most textbooks of medicine and public health: all interventions in patients who are or have been **symptomatic** (including rehabilitation)
- In review of 317 abstracts by Froom and Benbassat, 2001:
  - Tertiary prevention generally was **not** described as including:
    - Palliation of death
    - Reduction of specific complications or their mortality rates
    - Increase in quality-adjusted or disability-adjusted life years

Origins of the Three-Category Classification of Prevention, contd. (my critique)

- Reliance on symptomatology in classifications (as per slides above) is problematic
  - - Major diseases of current public health importance (e.g., HIV/AIDS, hepatitis C, coronary artery disease, hypertension, diabetes) can be asymptomatic for years as stealthily progress and damage body organs
  - - Other conditions (e.g., allergies, dermatitis) may be immediately symptomatic without serious morbidity
  - - Therefore, reduced reliance on symptoms in the classification of prevention could be helpful
    - - Relevant when symptoms are intrinsic to the definition of a stage of a specific disease, especially in advanced disease

Analysis of 3-Category Systems: Froom and Benbassat

- Froom and Benbassat (2001) reviewed 317 abstracts utilizing the terms primary, secondary, and tertiary prevention, and noted the following:
  - - Consensus in defining primary prevention as preventing a disease from occurring in the first place
  - - Overall, found inconsistent use of the terms secondary and tertiary (and sometimes even primary) prevention
  - - Concluded that these three categories are not specific enough to be appropriately used
  - - Reviewed alternative classification systems, and found limitations in all

Alternative Proposal of Froom and Benbassat: Substitute 7-Level Classification

- Level 1, **reducing exposure** to an etiologic agent
- Level 2, increasing resistance to the disease.
- Level 3, screening for risk factors for disease (in asymptomatic individuals) in order to reduce them.
- 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**
- Level 7, rehabilitation for "adjustment to irremediable conditions."

Critique of 7 "Level" Paradigm of Froom and Benbassat

- Advantages :
  - - Distinguishes exposure reduction as a separate level
  - - Includes resistance to acquiring disease despite exposure
  - - Includes screening for risk factors (meaning causative factors for acquisition or progression)
  - - Includes prevention of complications
  - - Addresses prevention or palliation of death
- Limitations:
  - - Does not constitute a continuum of successive prevention opportunities along the natural course of disease progression
  - - Limits methods of preventing disease acquisition (as a result of exposure) to increasing resistance
  - - Describes screening for risk factors but not for early disease
  - - Omits delay of the progression of chronic disease
  - - Expands to more than double the number of levels to remember

Another 3-level classification and critique

- Gordon (1983, from directorate of NIH) recognized difficulty of defining whether a status is a disease or a risk for one
- Proposed reclassifying prevention based on target population and risk, and eliminating all or most of "tertiary"
  - a) universal (for everyone)
  - b) selective (for groups at risk: occupational, age, pregnancy, etc.)
  - c) indicated (for those who already have an early condition)
- But still need to define a disease to understand its prevention
- Indications for the above categories could imply:
  - a) Preventing exposure in entire populations
  - b) Mitigating risk of acquiring disease for those exposed
  - c) Early treatment to prevent progression of disease

More recent 4-level alternatives

- Tannahill (1985) rejected 3-level model as **not following natural history** of disease; proposed 4 prevention "foci"
  - Preventing: a) 1st occurrence, b) avoidable consequences, c) **avoidable complications**, and d) **repeat occurrences**
- Jamoulle (conceived 1985, Belgian GP) **Quaternary prevention**
  - Defined as prevention of over-medicalization; added to primary, secondary, tertiary
- Beaglehole et al. Basic Epi (WHO 1993) described "**primordial prevention**," avoiding causative conditions
  - Expanded in Last's Dictionary of Epidemiology, 4th ed. (2001), to prevention of (presumably causative) risk factors, precursors, or conditions "known to increase risk of disease"; task of public health and health promotion; often cited
    - (But fits easily into either primary or stage 1 prevention)

More recent 4-level alternatives, contd., and use of term "stages"

- Davidson (2011, only on Academia.edu) added a "pre-primary" stage to classical 3, for staying healthy
  - Defined as adaptation to environment : …"**wellness** (mental, physical, social spiritual wellbeing) results"
    - (But what if the environment is unhealthy?)
- Some individual diseases (CHF, some malignancies) have long had identified stages, often 4 in number
  - A few theoretical articles now appearing classify stages for disease in general; fewer similarly classify prevention
  - At the time my 5-stage paradigm was conceived, 2006-09, prior use of term "stages" was not found for **prevention**

Stages of disease
A CDC 4-stage view

- A CDC online study course (*CDC: Principles of Epidemiology 3rd ed., 10/06 & 5/12)* lists 4 stages for most diseases:
  - **Susceptibility** (ends after exposure to disease; I start with the exposure)
  - **Subclinical disease**
    - "Latency" period, or "incubation period" for infection
    - Pathological changes develop but not detected
    - Ended by onset of symptoms (see below)
    - Duration may be seconds/minutes (bee sting -> anaphylaxis, or trauma -> tissue damage), days (COVID), or years (ASVD, AIDS)
  - **Clinical disease** (symptomatic; but advanced disease may be asymptomatic until complications; should sx define disease?)
  - **Recovery, disability, or death**

Recent 5-stage disease models

- Flores (quoting Suchman, 1979) (Only on Academia.edu, 17,000+ views), **5 stages in illness experience of patient**
  - Symptoms, sick role, medical care, dependent client role, recovery or rehabilitation; not about how the disease itself is progressing
- Okafo et al., 2009, Nigerian parasitologists (back to an interpretation of 1953 Leavell and Clark?)
  - General health promotion, specific prophylaxis, early diagnosis/treatment, limiting damage, rehabilitation
- Lumen Microbiology (undated, since 2010): 5 stages (for infections; used with classical 3 levels for prevention)
  - Incubation, prodromal, illness, decline, convalescent
- Kisling and Das, Jan. 2019, 5 disease stages
  - Underlying, susceptible, subclinical, clinical, recovery/disability/ death
  - Also 5 for prevention: classical 3 plus primordial, quaternary
  - But not clear how these correlate with the 5 disease stages

Now try out this as a new universal paradigm: 5 Stages of Disease Development

(Hattis and Law, 2009, published only online, not in a journal)

- The development/evolution of diseases (esp. chronic) generally involves 5 stages
- Each stage results from the last, and each lends itself to preventive interventions:
  - 1. Exposure to agents/causes of disease
  - 2. Acquisition of early disease due to exposure
  - 3. Progression of acquired disease from early to advanced state (when morbidity tends to begin)
  - 4. Complications resulting from advanced disease
  - 5. Death or Disability, generally from complications

In new Paradigm: Each of 5 Stages of Disease Development has its corresponding Stage of Prevention (Hattis and Law, 2009, published only online)

Stage #	Disease Development	Prevention of the Respective Stage
1	Exposure	Avoid Exposure
2	Acquisition (resulting from exposure)	Reduce Acquisition
3	Advancement/Progression (and transmission if communicable) (resulting from acquisition)	Interruption of Progression (start with screening for early disease) a) Cure the disease b) Slow the progression of disease c) Reverse the disease process d) Prevent transmission if infectious
4	Complications (usually resulting from advanced disease)	Avoidance of Complications a) Prevent initial complication b) Prevent recurrence of complication
5	Death or Disability (usually due to complications)	Prevention available even at this late stage a) Defer Mortality b) Rehabilitate Disability

Examples of the 5 Stages of Prevention

- **Stage 1:** Avoidance of exposure to agents of disease
  - Sexual abstinence; anti-smoking efforts
- Stage 2: Reduction of acquisition of disease (as a result of exposure)
  - Post-exposure prophylaxis; hepatitis B vaccine for drug users
- Stage 3: Interruption of the progression of a disease (which has been acquired); block dissemination through body and to others
  - Screening tests followed by treatment, e.g., HIV, lipid profile, BP
  - Some diseases can be cured or progression reversed, others slowed; transmission can be reduced for infectious processes
- Stage 4: Avoidance of complications (from progressed disease)
  - Prophylactic antimicrobials for AIDS patients; anticoagulants
- Stage 5: Delay of mortality, rehabilitation of disability, or palliative care for terminal disease
  - ICU care for stroke; physical therapy; hospice care

Stage 1: Exposure Avoidance

- Total avoidance of exposure should be **most effective prevention, but not always achievable**; partial avoidance is still Stage 1
- But **largest target population**: Entire population potentially exposed, or subgroups with greatest exposure
  - Can stratify by risks and prioritize interventions
  - Can identify degrees of exposure by survey data
- Exposure rate depends both on prevalence of agents of disease (microbes, toxins) and frequency rate of host contact
- Immunization can be Stage 1 , 2, or 4:
  - Stage 1 if prevalence of organism and therefore exposure declines due to herd immunity (MMR, polio); immunization benefits community
  - Stage 2 if prevalence continues, and used to mitigate exposure (influenza, rabies for veterinarians)
  - Stage 4 if used to prevent severe disease that can be considered a complication (Shingrix, Prevnar-13, Gardasil-9, COVID vaccines)
- Treatment of communicable diseases is Stage 3, but also Stage 1 prevention for exposed persons
  - Treatment reduces infectiousness, as in HIV; pre-exposure prophylaxis

Stage 1: Exposure Avoidance, contd.

- "Area under the curve" can calculate cumulative exposure
  - - Y axis = exposures; X axis = time (as with pharmacokinetics)
  - - Area = exposure * time (as in pack-years for smoking)
- Exposure avoidance, if excessive (avoiding normal risks of life), can actually be harmful to personal or public health
  - - Lockdowns in response to COVID-19 closed gyms, reduced social support, decimated some occupations
  - - Society survival requires some taking risks, e.g., police, military duty, health care during contagious outreak, and driving vehicles
- Some "risk factors" are markers associated with, rather than causes of disease; may not count as true exposure
  - Examples: CRP, depression for coronary heart disease
  - May be results of disease process, but still useful for screening

Stage 1: Exposure Avoidance, contd.

- **Must clearly define exposure, population at risk of exposure, and disease to which exposure contributes**
  - Will exposure to sexual risk of HIV be defined as anyone in the population who is sexually active, having unprotected or non-monogamous sex, having an HIV positive partner, or only if that partner has detectable viral load?
  - Will exposure to risk for smoking-related disease be defined as already smoking, or at risk for onset of smoking? Or will smoking be considered the disease?
- Target group for each intervention must be defined
- Exposure rate before and after intervention should be measured

Stage 2: Prevention of Acquisition as a Result of Exposure ("Harm Reduction")

- Generally next most effective option after Stage 1
  - May often be relatively inexpensive
- Target population: Exposed population (from Stage 1 of disease development)
  - Can identify by screening for exposure history
- **Can never be completely effective, because exposure persists, and no measures are 100% effective**
  - Examples: Exposure to COVID-19 while wearing mask; sexual exposure while using contraception or condoms
- Reducing exposure to risk of disease acquisition can be related to place, time, or behavior
  - Also includes interventions for persons genetically at risk

Stage 3: Detecting Early Disease and Treating to Interrupt Progression

- Similar to concept of secondary prevention
  - - Interventions to cure, slow, prevent, or reverse disease progression start with detecting early disease (those in whom Stages 1 & 2 failed)
  - - Interventions to prevent transmission of infection to others
- Target populations:
  - For screening: Test result or other evidence of early disease
    - - Particularly those exposed and lacking Stage 2 mitigations
    - - Testing should have high sensitivity, specificity, and predictive values; early disease often (but not always) asymptomatic
  - For treatment: those positive on screening
    - - Precise application depends on criteria for distinguishing early disease and advanced state
    - - For HIV, positive antibody test = acquisition; CD4<200 or AIDS-defining condition = advanced disease (monitor, screen for that too)

Stage 3: Interrupting Disease Progression, contd.

- Notes on Screening: As with traditional secondary prevention, can detect early disease, part of Stage 2
  - - But not always: can screen for exposure (Stage 1), for advanced disease (Stage 3), or for complications (Stage 4)
  - - **Must intervene after detection** for prevention to occur
- Goals of Stage 3:
  - **3a. Cure** of disease if possible
  - **3b. Slowing** of progression if progressive chronic disease
  - **3c. Reversal** of disease process if possible
  - **3d. Prevent spread to others** if disease is communicable
    - - As noted above, this is also **Stage 1** exposure prevention **for others**
    - - Stop external rather than internal progression/dissemination

Stage 3: Interrupting Disease Progression, contd.

- "Area under the curve" potentially useful here too
  - - "Viremia-years" correlate with mortality in HIV (*Mugavero et al., 2011)* and should correlate with total transmission
  - - Cholesterol or Hgb A-1c years may become important
- Particularly applicable to chronic diseases, and slowly-progressing infections
  - - Currently the predominant causes of death worldwide
- Less applicable to many acute illnesses and trauma
  - - Some conditions are sudden, have no gradual progression
  - - But some conditions that present as sudden emergencies had precursors (e.g., alcoholism and minor abuse before severe domestic abuse, allergic reactions predating anaphylaxis)
    - - Stages 1, 2, 4, and 5 still apply, even if not Stage 3

Stage 4: Preventing Complications from Advanced Disease

- When a chronic disease is advanced, a **complication** is often the cause of death or chronic disability
  - - For advanced atherosclerosis: M.I., stroke
  - - For AIDS: serious opportunistic infection, cancer
  - - For cancers beyond stage 1: organ failure, infection
- Stage 4a: Prevention of an **initial** complication
- Stage 4b: Prevention of **recurrence** of same complication
  - - Prevention of recurrent cardiac arrest has been called secondary prevention , tertiary prevention, or a 4th tier of prevention (*Tannahill)*
  - - Some medications (e.g., low-dose aspirin, beta blockers after M.I.) may prevent recurrences but not initial episodes

Stage 4: Preventing Complications from Advanced Disease, contd.

- Target population: Smaller, restricted to persons who already have advanced/progressed disease (as monitored in Stage 3)
- Interventions may range from simple medication to complex surgery, with corresponding cost ranges
  - Expensive: Stenting, coronary bypass surgery to prevent M.I.
  - Inexpensive: Trimethoprim-sulfa to prevent Pneumocystis or toxoplasmosis; low-dose aspirin, beta blocker to prevent 2nd MI
- Each disease may have multiple potential complications, of varied severity, with separate prevention strategies
- Some diseases have primary complications, & secondary complications resulting from primary; can define primary as disease
  - Strep A -> RF -> RHD
  - Viral hepatitis -> cirrhosis -> bleeding

Stage 5: Delaying/Reducing/Palliating Death or Chronic Disability from Complications, contd.

- Three alternative types of interventions for this stage:
  - Stage 5a: prevention (actually deferral; we all die) of death by treating the complication
  - Stage 5b: rehabilitation for disability
  - Stage 5c: palliative/end of life care
- Target population: Persons with significant complications (Stage 4 of disease development)
- Sometimes continuation of Stage 3 or 4 interventions may reduce mortality
  - Example (Thailand): Mortality rate of AIDS patients with TB reduced 84% if antiretroviral therapy (mainly used as Stage 3 and 4 to control HIV progression and complications) administered together with TB drugs

Stage 5: Delaying/Reducing Death or Chronic Disability from Complications, contd.

- Rehabilitation for a complication in which function can improve is restorative, but is also prevents chronic disability
  - If chronic disability has developed and cannot be reversed, rehab can prevent further deterioration, reduce dependence
- Although rehabilitation is only listed in Stage 5b, it can achieve earlier levels of prevention
  - Substance abuse treatment; or DVT prevention after injury
- Previous models omitted end of life care, but it can also be preventive (thus, **prevention available at all phases of care**):
  - Aims to prevent pain, distress
  - Settling affairs, advanced directives can reduce anxiety
  - Can save huge expenditures on futile care in last days of life

Application of model to specific diseases

STAGES		TYPE 2 DIABETES	HIV/AIDS	BREAST CANCER
1	Exposure Avoidance:	Healthy eating, limit simple carbohydrates, maintain healthy weight, exercise	Abstinence from sex (or screening and monogamy of seronegative partners), no injection drug use	Avoid known carcinogens (smoking, drinking ETOH), limit exogenous estrogens, avoid obesity, regular exercise
2	Disease Acquisition Reduction:	Weight loss, carbohydrate reduction, consider metformin if insulin resistance/pre-diabetes	Condom promotion, programs to discourage drug abuse, needle sharing, and PrEP	Tamoxifen, raloxifene or mastectomy as prophylactic treatment if BRCA gene (genetic exposure)
3	Interruption or Delay of Disease Advancement:	Anti-diabetic drugs, monitor hgb A-1C, FBS, proteinuria, lipids; bariatric surgery if indicated	Antibody screening, monitoring CD4, viral load; treatment with antiretrovirals	Detection of cancer by exams, mammograms, other imaging; biopsy; early surgery; hormone antagonism or ovarectomy if estrogen receptor
4	Avoidance or Delay of Disease Complications:	ACE Inhibitor/ARB to prevent renal sequelae, strict glucose control (insulin if necessary), lipid control, foot and eye care	Prophylactic treatment for opportunistic infections	Chemo/radiation therapy, mastectomy, follow up biannual mammogram post surgery, PET scan
5a	Delay of Mortality from Disease: Complications	Renal Dialysis, coronary stent or bypass	Intensive treatment for severe opportunistic infections	Full body radiation, bone marrow transplant

Stages of Prevention: economic tradeoffs

- Savings from early prevention:
  - Each stage prevents the stages that follow (a cost saving for early prevention)
  - Final stages of disease tend to be very expensive, so prevention at earlier stages saves those costs
- Savings from later prevention:
  - **Each consecutive stage is targeted at a smaller population**
  - Changing behavior of an entire population, e.g., to reduce risky sex or drug use (Stage 1) or to accept COVID vaccine (Stage 3) or wear masks (Stage 2) may be difficult and expensive per capita (if even possible)

Application of Stages of Prevention to Patient Counseling/Education

- Using current 3-level classification, patients at risk for HIV can be educated on:
  - Primary prevention to avoid getting the disease (e.g., safer sex)
    - **No distinction or preference** between avoiding exposure and harm reduction in the face of continued exposure
  - Secondary prevention to detect early disease (e.g., getting an HIV test)
    - **Often vague or silent** on interventions if disease is found
  - Tertiary prevention to prevent worsening of existing (symptomatic?) disease
    - **Not clear** from definitions at what point to intervene or what to teach; **not specifically targeted** at complications, mortality

Application of Stages of Prevention to Patient Counseling, contd.

- For HIV, using Stages of Prevention model, more options for personal behavioral decisions, based on where patients fall in stages of disease development, and what they are willing to do:
  - - **Stage 1:** avoid exposure to the disease (e.g., abstinence, testing partners and no sex if positive, not using drugs)
  - - **Stage 2:** avoid infection despite exposure (e.g., condoms, not sharing needles/needle exchange, pre-exposure prophylaxis)
  - - **Stage 3:** detect infection and treat it to avoid AIDS (e.g., get tested for HIV; take antiretroviral drugs if infected, which also reduces exposure of partners; prevention with positives)
  - - **Stage 4:** if already have AIDS, prevent complications (e.g., take antimicrobial drugs added to antiretroviral drugs; killed vaccines)
  - - **Stage 5:** post-complications (e.g., treat episode of opportunistic infection; palliation for AIDS-related terminal cancer

Application of Stages of Prevention to Public Health Planning

- Public health always involves limited budgets
  - Many diseases cause morbidity and mortality; which are worth investing in prevention, and at what stages?
- Example: You have $20,000/year to reduce first myocardial infarctions in a population of 10,000 adults with 35% elevated LDL, 4% 1st MIs/year; this money can (select, ID the stages):
  - - Educate 400 people @$50 to reduce their risk of hyperlipidemia, of whom 100 may change lifestyle and prevent 2-3 1st MIs/yr; or
  - - Pay for 1000 lipid profiles @$20, with referrals of 350 with high results to treatment, of whom 150 may follow through preventing 3-4 1st MIs/yr (but note lifetime treatment costs not included)
  - - Pay for 1 stent for a patient with unstable angina, prevent 1 1st MI

Critique of Stages of Prevention Paradigm

- Advantages of this classification system:
  - - Addresses disease prevention at 5 successive stages, **correlated with stages of disease**, providing a systematic approach to intervention
    - Primary, secondary, and tertiary prevention also successive, but not as progressive mathematically; identify fewer intervention categories
  - - Distinguishes between avoidance of exposure and mitigation of its effects
    - Splits current primary prevention into two stages
  - - Distinguishes among prevention of disease progression, of complications, and of death or chronic disability
    - Divides two vaguely defined categories (secondary and tertiary) into three more precise ones

Critique of Stages of Prevention Paradigm, contd.

Advantages, contd.:

- - Facilitates quantitative calculations and cost-benefit analysis
  - (See Appendix)
- - Can be used not only in health planning for populations, but also in counseling individual patients
- - Recognizes importance of asymptomatic but insidiously progressive disease
- - In final stage, provides alternatives of prolonging life, rehabilitating disability, or palliative care for terminal disease
- ***- Model provides prevention options for every specialty and aspect of medicine, and every patient***
  - ***- Not just a roadmap for Preventive Medicine specialty***

Critique of Stages of Prevention Paradigm, contd.

- Limitations of this particular classification system:
  - - Exposure to risk cannot always be avoided
  - - Not all diseases/conditions have preventable progression or complications; some lack progression at all (e.g., trauma)
  - - Use of term "stages" for disease development (though less so for prevention) may be confused with stage classifications of specific diseases (various cancers, CHF)
- Disadvantages of revising the classification of prevention:
  - - Will have difficulty competing with a paradigm over half a century old and in wide use
  - - New terms and 2 more categories to remember
    - Whereas primary, secondary, tertiary is as simple as 1, 2, 3

Critique of Stages of Prevention Paradigm, contd.

- Limitations of any classification system:
  - Cannot make universally applicable distinctions
    - The real world is messy
    - Prevention is complicated
  - The disease entity to be prevented, and each stage for each disease, must be clearly defined
    - Interventions to prevent a complication may be called primary prevention of the complication
    - Substance use can be considered as an exposure or as the disease in question
    - Lung cancer could be considered as the disease to prevent, or as a complication of lung disease from smoking

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Critique of Stages of Prevention Paradigm, contd.

More challenges for any classification system:

- A single intervention may be be useful in more than one stage, e.g., health education
- A single behavior may lead to multiple diseases (e.g., smoking)

- - In future, opportunities to integrate widely-used quality of life and longevity indicators
  - **QALY** (quality-adjusted life years) and **DALY** (disability-adjusted life years) could be used to measure effects of Stage 4 and 5 prevention
  - **YPLL** (years of preventable life lost) could highlight value in younger persons, especially Stages 1 and 2
- - Prevention of disease is not the whole story
  - Positive health promotion/wellness remains problematic in classifications for prevention of specific diseases

Is Disease Prevention Enough? What is Health in a Positive Sense?

- WHO formulation (1948):
  - Health is state of "complete physical, mental, and social well-being
  - Not merely the absence of disease and infirmity"
- Breslow (1999) proposed moving beyond disease prevention:
  - - Aiming for "the energy and reserves of health that permit a buoyant life, full of zest and the eager ability to meet life's challenges"
- Davidson (2011) suggested a pre-primary stage of prevention for wellness (as previously noted)
- Health promotion could be restored to primary prevention (as per Leavell and Clark, 1958 and 1965)
  - But nutrition, lifestyle are useful for prevention at every stage of disease
- Health promotion could be added to Stage 1, or add a 6th stage
  - Lifestyles avoiding exposure also promote wellness, but not a smooth fit
  - **OR**....

A Converse Paradigm: Stages of Health Promotion/Wellness – Open for Study

- Stage 1: Exposure to positive health influences*
  - E.g., health education
- Stage 2: Acquisition of healthy lifestyle practices due to the positive influences/education*
  - E.g., healthy diet, exercise
- Stage 3: Increase in measurable indicators of health and wellness due to the healthy practices*
  - E.g., optimal BMI, increase in strength and flexibility
- Stage 4: Achievement of defined health and wellness goals
  - Subjective, e.g., sense of wellbeing, fulfilling relationships, low stress
  - Objective, e.g., productivity, high cognitive function
- Stage 5: Optimal wellness?

*Interventions overlap with those for prevention of disease

Summary

- Traditional classification of prevention into primary, secondary, and tertiary categories has limitations, encounters criticisms
- A substitute paradigm has been presented: 5 Stages of Prevention, which correspond to and address the consecutive stages of acquisition and progression of chronic diseases:
  - 1) avoiding exposure to causative agents
  - 2) reducing acquisition of disease resulting from exposure
  - 3) interrupting advancement of disease that has been acquired
  - 4) preventing complications from advanced disease, and
  - 5) delay (or palliation) of death, or rehabilitation of disability, from complications.
- New model could serve as a tool for both population (public health) and personal health decisions and planning
- Precise definitions of the disease, exposure, acquisition, etc. needed
- Separate staging may be considered for health promotion/wellness

Interactive Exercise: What Stage of Prevention (or of Health Promotion)? (Hint: first define the disease)

- Condoms
- Needle exchange programs , and syringe/needle purchase at pharmacies (legal in California Jan. 2012)
- HIV screening with referral
- Antiretroviral drugs for patients with early
- HIV pre-exposure prophylaxis (PrEP), for high-risk exposed
- Low-dose aspirin for patients with hypertension or coronary disease
- Coronary care unit after myocardial infarction
- Passenger restraints
- Immunization
  - MMR
  - Rabies, for veterinarians
- Joining a gym

Discussion and Audience Critique

- What are the criteria that make a good model for classification of prevention?
- How do you currently utilize the concepts of primary, secondary, and tertiary prevention
  - How would the 5 Stages of Prevention model help or detract?
- What are your reactions to this proposal?
  - What are its strong and weak aspects?
  - What would you add or delete?
  - How could you utilize it in practice?

- APPENDIX

Calculations Facilitated by Stages of Prevention Model

- Every stage of disease, and of prevention, has a rate or ratio
- 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:
  - E/(p*t), the rate of exposures per defined population/year
  - A/E, the ratio of disease acquisitions per exposed persons/year
  - P/A, the ratio of progressed cases per acquired cases/year
  - C/P, the ratio of complications per cases of progressed disease/year
  - D/C, the ratio of deaths or disability cases per complications/year

Calculations Facilitated by Stages of Prevention Model, contd.

- The rate of any stage of disease will be the product of the rates of the stages up to that point; examples (note the algebraic cancellations):
  - The incidence of **ac**quiring the disease (Stage 2) is
    - A /(p*t) = E/(p*t) * A/E
  - The rate of progressed disease (Stage 3) is
    - E/(p*t) * A/E * P/A
  - The rate of a specific **c**omplication within the defined population (Stage 4) is
    - C/(p*t) = E/(p*t) * A/E * P/A * C/P
  - The mortality (death) rate (Stage 5) is
    - D/(p*t) = E/(p*t) * A/E * P/A * C/P * D/C
- Key: E = exposures, A = acquisitions, P = progressed cases, C = complications, D = deaths, p = popn., t = time

Calculations Facilitated by Stages of Prevention Model, contd.

- Example: the equation for rate of complications
  - C = E/(p*t) * A/E * P/A * C/P
- Start from exposure rate per population per year (E/p*t)
  - Subsequent stages of disease are determined by ratios of acquisitions/exposures (A/E), progressions/acquired cases (P/A), and complications/progressed cases (C/P)
    - These ratios are **multiplied** together with the exposure rate, to determine the rate of a particular stage of disease, because each is dependent on the previous stages
- Preventing any stage of disease also prevents the subsequent stages
  - For example, acquisition, progression, and complications will not occur if there is no exposure

Calculations Facilitated by Stages of Prevention Model, contd.*

- The rate of population unaffected by any stage of disease = 1 minus the rate of being affected
  - E.g., rate of those not exposed to disease = 1 – (E/p*t)
- Reduced disease rates (proportions of cases that were prevented) can also be calculated
  - Let proportion of reductions achievable by interventions at each stage be represented by E_r, A_r, P_r, C_r, and D_r, respectively
  - **Remaining disease rate after each intervention = baseline rate * (1 – reduced rate)**
    - E.g., remaining rate of disease exposure = E/p*t * (1 - E_r)
    - *Notations and equations changed from previous versions of these slides

Calculations Facilitated by Stages of Prevention Model, contd.

- Example of use of equations from last 2 slides:
  - C = rate of complications without interventions = E/(p*t) * A/E * P/A * C/P
  - C' = C prime, complication rate remaining after interventions = $E/p*t * (1 - E_r) * A/E * (1-A_r) * P/A * (1-P_r) * C/P * (1-C_r)$
    - Let baseline exposure rate be 50/1000/year with E_r (reduction in exposure rate) = 0.2; let A/E be 0.7 with A_r (reduction in acquisition rate) = 0.3; let P/A be 0.6 with P_r (reduction in progression rate) = 0.4; and let C/P be 0.4 with C_r (reduction in complication rate) = 0.5
      - Complication rate **without** preventive interventions = 50*0.7*0.6*0.4 = 8.4/1000/yr
    - Then reduced rate C' (C prime), combining all 4 interventions = 50*(1-0.2) * 0.7*(1-0.3) * 0.6*(1-0.4) * 0.4*(1-0.5) = 40*0.49*0.36*0.20 = 1.41/1000/year, an 83.3% reduction

Calculations Facilitated by Stages of Prevention Model, contd.

This demonstrates the benefit of combining prevention methods

Total health benefits from prevention interventions of different stages (note that this combines apples + oranges) =

$(p*t) * (E_r + A_r + P_r + C_r + D_r)$

Multiply instead of divide by population and time

Add rather than multiply effects of each stage

However, to be cost-effective, costs of reduction in rates and cases for each intervention should be compared

It may only pay to concentrate on one or two stages

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