TABLE 4-7 AGE-SPECIFIC CAUSES OF MORTALITY AND CORRESPONDING PREVENTIVE OPTIONS (*CONTINUED*)

Age Group	Leading Causes of Age-Specific Mortality	Screening Prevention Interventions to Consider for Each Specific Population
25–44	1. Accident	*As above plus consider the following:*
	2. Malignancy	• Readdress smoking status, encourage cessation at every visit (2,3)
	3. Heart disease	• Obtain detailed family history of malignancies and begin early screening/prevention program if patient is at significant increased risk (2)
	4. Suicide	• Assess all cardiac risk factors (including screening for diabetes and hyperlipidemia) and consider primary prevention with aspirin for patients at >3% 5-year risk of a vascular event (3)
	5. Homicide	• Assess for chronic alcohol abuse, risk factors for viral hepatitis, or other risks for development of chronic liver disease
	6. HIV	• Consider individualized breast cancer screening with mammography at age 40 (2)
45–64	1. Malignancy	• Consider prostate cancer screen with annual PSA and digital rectal exam at age 50 (or possibly earlier in African Americans or patients with family history) (1)
	2. Heart disease	• Begin colorectal cancer screening at age 50 with fecal occult blood testing, flexible sigmoidoscopy, or colonoscopy (1)
	3. Accident	• Reassess and update vaccination status at age 50 and vaccinate all smokers against *S. pneumoniae* at age 50 (6)
	4. Diabetes mellitus	• Consider screening for coronary disease in higher-risk patients (2,5)
	5. Cerebrovascular disease	• Consider screening for hepatitis C in adults born between 1945 and 1965 (7)
	6. Chronic lower respiratory disease	• Zoster vaccination at age 60
	7. Chronic liver disease and cirrhosis	• Begin mammography screening by age 50
	8. Suicide	
≥65	1. Heart disease	*As above plus consider the following:*
	2. Malignancy	• Readdress smoking status, encourage cessation at every visit (1,2,3,4)
	3. Cerebrovascular disease	• One-time ultrasound for AAA in men 65–75 who have ever smoked
	4. Chronic lower respiratory disease	• Consider pulmonary function testing for all long-term smokers to assess for development of chronic obstructive pulmonary disease (4,6)
	5. Alzheimer's disease	
	6. Influenza and pneumonia	• Screen all postmenopausal women (and all men with risk factors) for osteoporosis
	7. Diabetes mellitus	• Continue annual influenza vaccination and vaccinate against *S. pneumoniae* at age 65 (4, 6)
	8. Kidney disease	• Screen for dementia and depression (5)
	9. Accidents	• Screen for visual and hearing problems, home safety issues, and elder abuse (9)
	10. Septicemia	

Note: The numbers in parentheses refer to areas of risk in the mortality column affected by the specified intervention.

Abbreviations: AAA, abdominal aortic aneurysm; ATV, all-terrain vehicle; HPV, human papillomavirus; MMR, measles-mumps-rubella; PSA, prostate-specific antigen; STD, sexually transmitted disease; UV, ultraviolet.

5 Principles of Clinical Pharmacology

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Drugs are the cornerstone of modern therapeutics. Nevertheless, it is well recognized among physicians and in the lay community that the outcome of drug therapy varies widely among individuals. While this variability has been perceived as an unpredictable, and therefore inevitable, accompaniment of drug therapy, this is not the case. The goal of this chapter is to describe the principles of clinical pharmacology that can be used for the safe and optimal use of available and new drugs.

Drugs interact with specific target molecules to produce their beneficial and adverse effects. The chain of events between administration of a drug and production of these effects in the body can be divided into two components, both of which contribute to variability in drug actions. The first component comprises the processes that determine drug delivery to, and removal from, molecular targets. The resulting description of the relationship between drug concentration and time is termed *pharmacokinetics*. The second component of variability in drug action comprises the processes that determine variability in drug actions despite equivalent drug delivery to effector drug sites. This description of the relationship between drug concentration and effect is termed *pharmacodynamics*. As discussed further below, pharmacodynamic variability can arise as a result of variability in function of the target molecule itself or of variability in the broad biologic context in which the drug-target interaction occurs to achieve drug effects.

Two important goals of the discipline of clinical pharmacology are (1) to provide a description of conditions under which drug actions vary among human subjects; and (2) to determine mechanisms underlying this variability, with the goal of improving therapy with available drugs as well as pointing to new drug mechanisms that may be effective in the treatment of human disease. The first steps in the discipline were empirical descriptions of the influence of disease on drug actions and of individuals or families with unusual sensitivities to adverse drug effects. These important descriptive findings are now being replaced by an understanding of the molecular mechanisms underlying variability in drug actions. Thus, the effects of disease, drug coadministration, or familial factors in modulating drug action can now be reinterpreted as variability in expression or function of specific genes whose products