Cultural and Genetic Diversity in America: The Need for Individualized Pharmaceutical Treatment

by

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About the National Medical Association (www.nmanet.org)

The National Medical Association (NMA) is the collective voice of African American physicians and the leading force for parity and justice in medicine and the elimination of disparities in health. The National Medical Association is a 501(c)(3) national professional and scientific organization representing the interests of more than 25,000 physicians and their patients. Established in 1895, NMA is committed to 1) preventing the diseases, disabilities and adverse health conditions that disproportionately or differentially impact African American and underserved populations, 2) supporting efforts that improve the quality and availability of health care to poor and underserved populations, and 3) increasing the representation and contribution of African Americans in medicine.

About the National Pharmaceutical Council (www.npcnow.org)

Since 1953, the National Pharmaceutical Council (NPC) has sponsored and conducted scientific, evidence-based analyses of the appropriate use of pharmaceuticals and the clinical and economic value of pharmaceutical innovations. NPC provides educational resources to a variety of health care stakeholders, including patients, clinicians, payers and policy makers. More than 20 research-based pharmaceutical companies are members of the NPC.
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This report reviews the environmental, genetic and cultural factors that underlie variations in drug response among different population groups. Population groups that have been conventionally defined along racial and ethnic categories comprise important subgroups whose special needs and drug responses traditionally have been undervalued or ignored. Given the genetic and cultural variation among individuals in these groups, drug management policies in both public and private pay pharmaceutical programs must be flexible enough to accommodate patients’ specific needs.

The factors determining population variations in response to medications are complex and interdependent. Environmental factors (e.g., climate, smoking, alcohol consumption) may have a profound effect on drug metabolism. Biologic factors such as genetic polymorphisms (naturally occurring variations in the structures of genes, drug metabolism enzymes, receptor proteins, and other proteins involved in drug response or disease progression), age, and gender have significant influence and may require the use of alternate drugs or dosages in patients of different racial and ethnic backgrounds. Genetic research in the past few decades has uncovered significant differences among populations in the metabolism, clinical effectiveness, and side effect profiles of therapeutically important drugs; however, most of the research applies to African Americans, Asians, and Caucasians. Fewer studies have specifically targeted Hispanics who, according to the 2000 U.S. Census, represent the second-largest ethnocultural group.

Cultural or psychosocial factors have been documented to affect a patient’s adherence to, and therefore the effectiveness of, drug therapy. For example, trust and respect for patients and their health beliefs and practices, as well as communications issues, have been found to influence adherence to medication regimens. Patients’ beliefs about the nature of disease, acceptance of side effects, and preferences regarding herbal or traditional therapies may be influenced by a range of sociocultural influences, including gender, socioeconomic class, education, immigrant status, and religion, all of which must be taken into account. Additionally, communications barriers may lead to incorrect interpretations of diagnoses and instructions regarding treatment. A frequently overlooked and underemphasized barrier, especially in the elderly and in underrepresented minorities, is inadequate health literacy. This comprises their ability to understand and follow through on health information matters. Of greater significance is the recognition of the considerable skills that these patients have in concealing their poor health literacy. Taken together, these variables dictate that in order to be effective, therapy must be individualized.
**Recommendations**

Health care policy makers and providers should pay attention to the need to individualize drug therapy for specific population groups. The following recommendations could benefit the quality of care for racial and ethnic subpopulations and may also help to control health care costs.

1. **Health care institutions should implement cost containment practices that are broad and flexible enough to enable rational choices of drugs and formulations for all patients, regardless of race or ethnic origin.**

2. **Physicians should give individualized treatment to each patient and prescribe drug therapy that takes into account racial or ethnic origin and sociocultural influences.** Physicians should also be alert to atypical drug responses or unexpected side effects (especially with cardiovascular or psychotropic agents) when they treat patients from diverse racial and ethnic backgrounds. Patients may not be taking the medication properly due to misunderstood instructions, or misperceptions about Western medicine or the severity of the disease. Dosage adjustments may be required in some patients if supported by pharmacological evidence.

3. **Pharmaceutical companies should continue to include significant numbers of patients representing varied racial and ethnic groups in drug metabolism studies and clinical trials.** Most companies test and evaluate new pharmacological compounds on numerous population subgroups. Inclusion of different racial and ethnic populations in clinical trials is likely to reveal drug actions and side effects specific to these groups, and may also to lead to the discovery of therapies of specific advantage to patients of varied racial and ethnic backgrounds.

4. **Hospitals, managed care groups, and other providers of health care services should endeavor to employ practitioners who are racially and ethnically representative of the patient population being served.** Provider organizations should develop and institute specific training in cultural competence for all practitioners who have direct patient contact—especially physicians, pharmacists, nurses, and physician assistants.

**Toward Individualized Therapy**

Race and ethnicity have been used as factors in determining if an individual will respond in the expected way to a given drug therapy. However, race is an imprecise substitute for genetic variations that an individual may or may not possess. Technological advances in the wake of the Human Genome Project will eventually enable us to move beyond flawed concepts of race and to tailor drug therapy precisely to each patient. It is now possible to take a genetic “fingerprint” of an individual and precisely determine the presence of polymorphisms in the genes known to be involved in drug interaction. Instead of a person's racial category being a risk factor for the possession of polymorphisms involved in drug response, a genotypic profile can determine with certainty whether or not the individual possesses these polymorphisms.

In the future, drug treatment will be individually tailored rather than race-based. Genetic fingerprinting using DNA arrays is already practical, but the knowledge base relating genomic variations to drug response and disease progression has not been developed. Studies in which DNA fingerprints are correlated with data present in medical records about medical history and drug response will have a profound impact on the ways in which new drugs are developed and used.
However, treating individuals involves more than awareness of genetic variations. Apart from the physiological complexities associated with appropriate prescribing for different racial and ethnic groups, practitioners face the added challenge of delivering effective pharmaceutical care to people within a psychosocial context appropriate to their culture and level of health literacy. The great diversity in our patient population demands a framework in which the practitioner can approach all patients, regardless of racial, ethnic, or sociocultural background, as egalitarian partners in care. Although any discussion of sociocultural competence can list examples of our differences, it is important to remember the many similarities exist among diverse peoples. All patients seeking care have recognized a need for that care. All share feelings of need, fear, mistrust, lack of control, hope, and disconnection from their normal world of health. When these feelings are acknowledged and respected by a culturally competent practitioner, partnerships can be built in which any cultural health belief or treatment preference can be discussed.
Individual genetic polymorphisms are naturally occurring variants in the structures of genes, drug metabolism enzymes, receptor proteins, and other proteins involved in disease progression. These polymorphisms change gradually in prevalence across continents and do not separate populations into clearly demarcated groups that correspond to popular ideas of race.

The most obvious manifestations of racial differences—skin color, cranial features, etc.—are superficial characteristics that have little relevance to drug responses or to the progression of complex diseases such as diabetes mellitus, coronary heart disease, etc. It should be emphasized that humans are one species. Although we have evolved as geographically separated groups, our differences have not yielded large variations in genetic composition. Those genetic differences that do exist reflect variations from only a small number of genes. Therefore, “race” is an imprecise substitute measure of genetic differences among populations.

The idea of race is extremely complex. It refers to a grouping of humans into specific categories that have no underlying biological underpinning. Yet, because the groupings are largely based on physically visible features, race appears to be real. This may explain why race as a flawed concept is difficult to eradicate from usage—in both scientific and general discourse. For example, skin pigmentation has been used as a marker for race (white, black, red, yellow). But skin color alone is quite deceptive, as the same range of colorations can be found among persons from different population groups. For example, those from certain Asian backgrounds can be as dark as those from Africa. And those from African ancestries can be as light as those whose ancestry can be traced to Europe.

Historically, the categorization of human beings according to physical attributes linked to geography and later termed race can be traced back to the eighteenth century. Not only were varieties of humans described, but also a hierarchical ordering was ascribed to these varieties, where one group (those who could later be called “white”) was considered the most superior. Therefore, embedded in the idea of race is this notion of the ascendancy of some groups over others.

In the U.S., criteria used to identify “racialized” groups have not been based solely on biological markers, but also on the idea of ethnic or cultural indicators. For example, Hispanics comprise a group of individuals who generally share a linguistic heritage but who represent multiple nationalities and racialized groupings, including white, black and indigenous Indians.

The terms ethnicity and culture have also been subject to conceptual misunderstanding and thus require more precise and coherent definitions if they are to be useful. Together they refer to combinations of “socioeconomic, religious, and political qualities of human groups, including language, diet, dress, customs, kinship systems, and historical or territorial identity.”

Like “race,” both ethnicity and culture are also subject to social constructions whose borderlines are not easily mapped. They reflect our own projections and are also subject to individual fluidity. One can inhabit multiple cultural or ethnic identities and move between them depending on need or circumstance. Thus, we must resist any temptation to view these concepts as having material reality. The conditions and ways certain individuals or groups can be assigned to a specific ethnic or cultural group must be specified. For example, we should speak not of Hispanic culture but rather of cultural beliefs held by certain populations of persons from specific areas, say Puerto Rico or El Salvador.
Research in the last 35 years has uncovered varying distributions of genetic polymorphisms in enzymes and receptors associated with drug metabolism. These are reflected in differences among population groups in clinical responses to drugs and in drug side effects. For example, black and white patients have been shown to differ significantly in their responses to beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, and diuretics used either alone or in combination for the treatment of high blood pressure. Some populations of Chinese are considerably more sensitive than whites to the effects of the beta-blocker propranolol on heart rate and blood pressure. African Americans and Chinese Americans metabolize nicotine more slowly than do whites, and genetic variations associated with slower nicotine metabolism are more common in some Asian populations. As compared to some whites, certain Asian groups are more likely to require lower dosages of a variety of different drugs used to treat mental illness, including lithium, antidepressants, and antipsychotics.

Concepts of identity based on racial markers, ethnicity or culture may be useful when discussing trends among populations, but they cannot predict individual behavior. We cannot rely on a form of racial profiling – using visible or socially constructed markers, such as skin pigmentation, eye-shape, language use, or health beliefs, to accurately identify the presence or absence of polymorphisms in drug-metabolizing enzymes or drug receptors. The usefulness of these concepts lies in their ability to increase the clinician’s awareness of differences and the threshold for considering alternative treatment modalities, but not for limiting options in diagnosis or treatment for an individual patient. To do otherwise would be to stereotype in ways that could, in turn, contribute to the inequities reflected in health disparities. In addition to the physiological complexities associated with appropriate prescribing for different racial and ethnic groups, practitioners face the added challenge of delivering effective pharmaceutical care to these individuals within a psychosocial context appropriate to their cultural beliefs and practices. The great diversity in our patient population demands a framework in which the practitioner can approach all patients as egalitarian partners in care, regardless of cultural background.

Although any discussion of sociocultural competence can list examples of our differences, it is important to remember the many similarities among diverse peoples. All patients seeking care have recognized a need for that care. All share feelings of need, fear, mistrust, lack of control, hope, and disconnection from their normal worlds of health. When these feelings are acknowledged and respected by a culturally competent practitioner, partnerships can be built in which any cultural health belief or treatment preference can be discussed.
Purposes of This Report

This report 1) reviews the interrelated causes of variability in response to medicines among racial and ethnic groups; 2) discusses examples of drugs to which racial and ethnic groups respond differently; 3) discusses the implication for pharmaceutical cost containment practices; and 4) makes recommendations for health care providers and policy makers who are responsible for clinical decisions affecting patient care.

Terms Used in This Report:

- **Ethnicity and Culture** – Refer to combinations of socioeconomic, religious, and political qualities of human groups, including language, diet, dress, religions, customs, beliefs, worldviews, kinship systems, and historical or territorial identity.

- **Extensive Metabolizer** – An individual who metabolizes a drug at a normal rate of efficiency.

- **Health Literacy** – The ability of an individual to understand and follow through on health information matters.

- **Pharmacodynamic Properties** – Effect of a drug on the body.

- **Pharmacogenetics** – The study of variations in a gene on drug response.

- **Pharmacogenomics** – The study of variations in multiple genes on drug response.

- **Pharmacokinetic Properties** – Absorption, distribution, metabolism, excretion of a drug.

- **Polymorphisms** – Naturally occurring variations in the structures of genes, drug metabolism enzymes, receptor proteins, and other proteins involved in drug response or disease progression.

- **Poor Metabolizer** – An individual who does not metabolize a drug efficiently.

- **Racial Group** – A group of people who share socially constructed differences based on visible characteristics or regional linkages.
Disparities in the quality of medical care provided to patients representing different racial and ethnic groups have been extensively documented. The recent report of the Institute of Medicine (IOM), "Unequal Treatment: Confronting Racial and Ethnic Disparities in Healthcare," illustrates in detail that racial and ethnic disparities in health care do exist and are prevalent in both the treatment of medical illness and in the delivery of health care services to minorities in the U.S.

Of greater significance is the finding that these disparities still exist even after adjustment for differences in socioeconomic status, insurance coverage, income, age, co-morbid conditions, expression of symptoms, and access-related factors. These disparities are not confined to any one aspect of health care, and can also be found in the delivery of pharmaceutical services.

Most studies have focused on African Americans, but other studies have shown that Hispanic and Asian Americans are similarly affected. Patients in these groups receive less intensive medical treatment than the nation as a whole, including fewer vaccinations, less drug therapy for pain, fewer antiretroviral drugs for HIV/AIDS, and fewer antidepressants. Low-income Hispanic children with asthma were less likely than their white and African American counterparts to have taken inhaled beta-agonist or anti-inflammatory medications before hospitalization.

African American and Hispanic patients with severe pain are less likely than white patients to be able to obtain commonly prescribed pain medicines, because pharmacies in predominantly non-white communities do not carry adequate stocks of opiates. Other studies have revealed undertreatment of Hispanics and African Americans for pain from fractures, inadequate management of postoperative pain in non-white patients, and a lower likelihood of curative surgery for cancer in African Americans than in whites of equivalent socioeconomic status.

Disparities in the quantity and quality of care received can stem from a variety of causes. There are often communication obstacles between a patient and provider that can be due to language, a difference in cultural background, preconceived stereotypes, or incorrect assumptions about what the patient does and does not understand about their health. This can lead to noncompliance with prescribed treatments and ineffective management of disease.
The demographic changes anticipated over the next decade magnify the importance of these disparities. According to the 2000 census, racial and ethnic groups other than “white” make up almost one third of the U.S. population (Figure 1). African Americans and Hispanics represent a growing percentage of the urban population in the U.S. These groups constitute the new urban majority in cities such as Washington, Detroit, and Los Angeles.

A disproportionate fraction of these urban Americans depend on Medicare or Medicaid as their sole health care payer. As drug coverage policies within these programs evolve, they must account for the special needs of a growing percentage of the patient groups they are intended to serve. These groups may be further disadvantaged if they do not have access to individualized care with appropriate pharmaceuticals.

**Common Cultural Themes and Health Beliefs of the Dominant Society in the U.S.**

Although not universal, there are some common themes and health beliefs of the dominant society in this country. These broad concepts are only crude indicators and certainly do not characterize the thinking of all Americans. On the other hand, neither are they necessarily held only by the non-Hispanic white majority. The authority of the dominant society has been internalized by many groups. In addition to ethnic and cultural differences, generational and gender factors are also likely to be important determinants of health beliefs for Americans. Some common themes include:23

- A relative intolerance of pain. Unlike many other culturally held beliefs, where pain is seen as part of life, the typical Western attitude toward pain is to relieve it as soon as possible.
- A high expectation that one’s disease can and will be cured or at least “managed.”
- The need to leave the doctor’s office with a prescription.
- The belief that medications should be powerful but free of risk, and that strong medications should be available only by prescription.
- A belief in the magic of high technology and one’s entitlement to it.
- The belief that management of microbes is more important than bolstering resistance to them.
- The belief that the physical aspects of disease are separate from its emotional and spiritual dimensions.
- The belief that the body is a machine and that proper maintenance (diet, exercise) will prolong its useful life; and that technology enables replacement of defective or worn out parts.
- A belief that mental diseases are not as important, or as “real” as somatic diseases.
Disparities in Cultural Competency

At the most basic level, care may be compromised due to cross-cultural language and other communication barriers. For instance, among adult Hispanics with asthma who spoke only Spanish, there was a greater likelihood of missed follow-up appointments, non-adherence to medications, and emergency room visits among those whose physician spoke only English compared to those with bilingual physicians.24

Culturally shaped beliefs play a vital role in determining whether an explanation of illness or treatment makes sense. Indigenous systems of health beliefs, practices and medicines exist in all societies and exert profound influence on patients’ attitudes and behaviors.25,26 Since cultural beliefs may greatly influence treatment outcomes, it is important to assess the likelihood that a patient will act on these beliefs.

One strategy for improving cultural competence among health care providers is for health care providers themselves to better reflect the diversity of those they serve. One in four Americans is non-white, Hispanic, or Native American, but fewer than 10 percent of those in the health professions workforce represent these minority groups.27 African American and Hispanic physicians make up only 2.2 percent and 2.8 percent of all practicing physicians in America respectively, a woefully inadequate number to care for these groups, each of which exceeds 10 percent of the population. Health care provider organizations that effectively close this gap will achieve a competitive advantage in serving the needs of their ethnically diverse customers.

While ideally patients would be matched with providers of similar backgrounds, realistically we must find ways to train all health care providers to be sensitive to the sociocultural beliefs that may influence the effectiveness of any prescribed treatment regimen. A mismatch between lay and professional perspectives often results in patients’ dissatisfaction with treatment.28,29,30

Disparities in Health Literacy

Health literacy refers to the set of skills needed to read, understand, and act on basic health care information. Over 90 million adults in the U.S. have low health literacy skills, with limited ability to read and understand the instructions contained on prescriptions or medicine bottles, appointment slips, informed consent documents, insurance forms, and health educational materials.31

Members of socioculturally disadvantaged groups, especially those for whom English is a second language, are more likely than educated or socioeconomically advantaged adults to have limited literacy skills, thus impacting their ability to understand and follow prescribed health care regimens.31,32 There is a relationship between low literacy and self-management skills, including the ability to take medications properly. For example, asthma patients with lower literacy levels were found to have a relatively poorer technique when using their metered-dose inhaler.33

In another case, many patients receiving acute care at two urban hospitals were unable to read and understand basic medical instructions.34 Forty-two percent did not understand directions for taking medication on an empty stomach, and twenty-six percent did not understand information on scheduling their next appointment. Thirty-five percent of the English-speaking patients had inadequate or marginal functional literacy, but for the Spanish-speaking patients, the figure was even higher (62 percent).

For some serious chronic diseases, such as diabetes, low health literacy poses a compounded threat to overall health. Because self-management relies heavily on printed instructions, literacy is a key factor. A study of low-income African American patients with non-insulin-dependent diabetes found the functional health literacy level was adequate in only 25 to
47 percent of patients at diabetes clinics. Another study found that patients with inadequate health literacy were more likely to have poor control of their blood sugar levels and to report eye problems (usually involving blood vessels of the retina) which may progress to blindness.

Furthermore, low-literacy patients did not readily identify themselves; 43 percent of those with low health literacy denied having any difficulty in reading; 54 percent of those with low-literacy said they did not usually ask anyone to help them read medical forms, and only 29 percent reported asking someone (usually relatives or neighbors) to help them read the written materials given to them. Such patients were least likely to ask their physician for help.

Standard patient informational practices have been shown to be insufficient to overcome the barriers posed by low health literacy. Often, health educational materials are written at an inappropriate reading level, especially for minority groups in which English may be a secondary language. For example, in one study, although many American Indian diabetic patients scored at a 5th grade reading level, the diabetes education materials designed for them were written at a 10th grade reading level. In another example, less than half of the cancer education materials specifically targeting African Americans reflected the cultural values of African Americans, and few were written at a reading grade level for those with low literacy skills.

Although much effort has been devoted to improving the quality of written information, improvement in oral and visual communication to convey necessary medical information has received inadequate attention. Health care practitioners are therefore challenged to communicate clearly and concisely with patients and to take a patient-focused approach to care. This also involves perceiving and surmounting less visible barriers such as patient confidence, shame, or fear. Practitioners must be able to communicate effectively across cultural, socio-economic, educational, and geographical differences.

The Language of Medicine

Due to the highly technical nature of the language of medicine, patients may not understand seemingly common medical terms. Compounding the problem is the skill of patients in concealing their poor health literacy. They usually will not acknowledge their deficiency due to feelings of shame, even though it interferes with their health.

In a study of health vocabulary, only 13 percent of participants understood the meaning of the word “terminal,” only 18 percent understood “malignant,” and only 35 percent understood “orally.”

In a study of Medicare patients, striking deficiencies were found in their understanding of critical areas of health care:

- 48 percent did not understand written instructions to “take medicine every six hours.”
- 68 percent could not interpret a blood sugar level.
- 27 percent did not understand “take medicine on an empty stomach.”
- 27 percent could not identify their next appointment.
- 100 percent could not understand a statement of Medicaid rights written at a 10th grade reading level.
The factors contributing to variability in drug response are complex and interrelated (Figure 2). Differences in drug response among racial and ethnic groups are determined by environmental, genetic and cultural (in this context, psychosocial) factors. These factors may operate independently or they may interact dynamically and synergistically.

**Environmental Factors**

Environmental factors – diet, climate, smoking, alcohol, drugs, pollutants, and environmental toxins – may cause wide variations in pharmacological response within an individual and even wider variations between groups of individuals. Several of these factors can operate simultaneously in the same individual, thus affecting the processes of drug absorption, distribution, metabolism, excretion, and receptor interaction in different ways and to different degrees.

Differences in diet may significantly alter the metabolism rate or the amount of a drug present in the blood among different ethnic populations. Studies comparing the metabolism of a specific drug (antipyrine) between Asian Indians in rural villages and Indian immigrants in England demonstrated that, as immigrants adopted the lifestyle and dietary habits of the British, their drug metabolism accelerated. Similar findings have been observed among Sudanese and Western Africans.

Additionally, smoking can be an important factor in determining response to pharmaceuticals. This is of particular note since cigarette smoking accelerates the metabolism of many prescription drugs commonly used to treat chronic diseases such as asthma and high blood pressure, thereby making them less effective. However, some drugs used to treat these conditions are not affected by smoking; prescribing can be individualized to use these agents in smokers.

Smoking-related disease and mortality is disproportionately prevalent among African Americans. Up to 45 percent of urban-dwelling African Americans reported that they were smokers, compared with 25 percent for the general population. The smoking patterns of African Americans are very different from those of whites. African Americans smoke fewer cigarettes per day (15 vs. 25 for whites), prefer mentholated and higher tar or nicotine cigarettes, and are more likely to smoke within 10 minutes of awakening. African Americans also metabolize nicotine more slowly and have higher serum nicotine metabolite levels per cigarette smoked than whites. They may also develop dependence at lower levels of smoking, making it more difficult for them to quit.

Adapted from Poolsup et al
success rate for blacks who try to quit smoking is 34 percent lower than for whites. Sustained release bupropion has been found to be particularly effective as an adjunct to help African Americans quit smoking. The drug seems to alter nicotine metabolism in blacks more than whites, in addition to its known effect as an antidepressant.

**Genetic Factors**

Although age and gender affect drug response, the primary biological factor impacting the effectiveness of properly followed treatments is genetics. Studies of twins and blood relatives have shown that genetic differences are the major biological factors determining the normal variation in drug effects, and are responsible for many differences in drug activity among healthy subjects studied under carefully controlled environmental conditions. More than 100 examples have been documented in which inherited individual traits were implicated in atypical, exaggerated responses to drugs, novel drug effects, or lack of effectiveness of drugs.

The genetic makeup of an individual may change the action of a drug in a number of ways as it moves through the body. Genetic factors may influence a drug’s action by altering its pharmacokinetic properties (absorption, distribution, metabolism, excretion) or pharmacodynamic properties (effect on the body). Clinically, there may be an increase or decrease in the intensity and duration of the expected typical effect of the drug.

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**Human Migration: The Distribution of Genetic Polymorphisms**

Anatomically modern humans evolved in Africa about 100,000 years ago. Some of these people migrated from East Africa into Eurasia, and subpopulations spread east into southern Asia. Australia was inhabited around 50,000 years ago (and subsequently remained completely isolated from the rest of the world until the late 18th century). Modern humans first inhabited Western Europe about 40,000 years ago. The northern latitudes were penetrated quite late. Following the habitation of Siberia 15,000 to 35,000 years ago, humans spilled into Alaska and rapidly occupied the whole of the North and South American continents. The Pacific islands were colonized by peoples originating in South China beginning about 5500 years ago and continuing into the historic period. Human populations continued to migrate throughout prehistoric and historic times, displacing, coexisting, or intermixing with indigenous peoples. The result is that there are no distinct geographic boundaries between genetic variations; rather, there are gradations in the prevalence of polymorphisms across geographical distance.

Two factors led to genetic differences among peoples and hence potential differences in drug response. First, genetic mutations continued to arise spontaneously in populations that were geographically isolated from one another. These mutations were subject to environmental selection. Second, because these population movements were initiated by subgroups of people, they tended to represent only a particular subset of the genetic polymorphisms that were present in the entire human population. The smaller the migrant subgroup, the more genetically distinct it would be from other subgroups – a phenomenon called the “founder effect” – leading to distinct patterns of polymorphisms in the descendent populations.

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The study of genetically determined variations in drug response is called pharmacogenetics. Variations in drug response are caused by gene polymorphisms, which are naturally occurring variations in the structures of genes, drug metabolism enzymes, receptor proteins, and other proteins involved in drug response or disease progression. Pharmacogenetics traditionally meant the study of polymorphisms in individual genes. This field now has broadened into pharmacogenomics, which examines the effects of multiple genes on drug response. In pharmacogenomics, large arrays of genes are studied in parallel, so that the entire spectrum of genes that determine the response to a particular drug can be examined at one time.

Clinical relevance of genetic differences (polymorphisms)

Common polymorphisms in drug metabolism genes have received the most attention because they affect the metabolism of many clinically important and commonly used drugs. Polymorphisms in these genes most often affect drug metabolism by reducing it, sometimes by disrupting it, and occasionally by enhancing it. Individuals who do not metabolize a certain drug efficiently are called “poor metabolizers,” as opposed to normal or “extensive metabolizers.”

Poor metabolizers process drugs over a longer period of time, increasing not only the length of time the body is exposed to a given drug, but also the concentration of the drug in the bloodstream, creating the equivalent of an overdose. Poor metabolizers generally do not experience increased effectiveness because dosages are normally targeted to have optimum efficacy and higher dosages do not further increase the effect. However, they often do experience increased adverse events as if they had been given a dose that is too strong. In sum, poor metabolizers have a decreased therapeutic ratio (efficacy:toxicity) for the specific drug.

It is important to note whether a given polymorphism has clinical relevance in drug therapy. Several factors determine the clinical importance of a genetic polymorphism:54

• First, polymorphisms only have clinical importance when they result in large differences between poor metabolizers and extensive metabolizers.

• Second, differences are relevant chiefly if the drug has a small therapeutic index, i.e., the ratio of its therapeutic effect to its adverse effects.

• Third, if physicians adjust drug dosage based on the therapeutic effect (as is common practice with drugs to treat high blood pressure), then differences between poor and extensive metabolizers are automatically corrected.

• Fourth, the clinical implications are broader for widely prescribed drugs such as beta-blockers and tricyclic antidepressants because more patients in more population subgroups are affected.

Most pharmacogenetic studies have concentrated on several groups of drugs and their activity in certain populations. These drug groups include cardiovascular agents and central nervous system agents (Table 1). Cross-racial variability in the action of drugs in these categories is clinically significant and results from differences in pharmacokinetic or pharmacodynamic factors, or in the pathophysiology of disease.

Factors Determining the Clinical Importance of a Genetic Variation in Drug Metabolism54

1. There is a notable difference between extensive metabolizers and poor metabolizers in how the drug affects the body.

2. The drug has a narrow therapeutic index.

3. The dosage of the drug is not individually evaluated on the basis of the therapeutic effect.

4. The drug is widely used by many physicians, not only by clinical specialists.
Table 1. Drug Showing Varying Effects Among Racial and Ethnic Groups

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comparison Groups</th>
<th>Blood Concentration of Drugs</th>
<th>Clinical Response</th>
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<tbody>
<tr>
<td><strong>ACE INHIBITORS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enalapril</td>
<td>Blacks vs. Whites</td>
<td>N/A</td>
<td>High blood pressure and hospitalization for heart failure is reduced in whites but not in blacks with left ventricular dysfunction</td>
</tr>
<tr>
<td>Captopril</td>
<td>Blacks vs. Whites</td>
<td>N/A</td>
<td>Effect in lowering blood pressure is greater in whites</td>
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<tr>
<td><strong>BETA-BLOCKERS</strong></td>
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</tr>
<tr>
<td>Isoproterenol</td>
<td>Black vs. White men</td>
<td>N/A</td>
<td>Relaxing of the blood vessels is markedly lower in blacks</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Chinese vs. Caucasians</td>
<td>Lower in Chinese</td>
<td>Chinese are twice as sensitive to effects on blood pressure and heart rate</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Blacks vs. Whites</td>
<td>N/A</td>
<td>Effect in lowering blood pressure is greater in whites</td>
</tr>
<tr>
<td><strong>CALCIUM CHANNEL BLOCKERS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>South Asians vs. Caucasians</td>
<td>Threefold higher in South Asians</td>
<td>N/A</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>Koreans vs. Caucasians</td>
<td>Greater in Koreans</td>
<td>N/A</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>Nigerians vs. Caucasians</td>
<td>Greater in Nigerians</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>DIURETICS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Blacks vs. Whites</td>
<td>N/A</td>
<td>71% of blacks achieved blood pressure goal vs. 55% of whites in Veterans Administration study</td>
</tr>
<tr>
<td><strong>CENTRAL NERVOUS SYSTEM AGENTS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Asians, (Indian, Pakistani) vs. Whites (English)</td>
<td>Greater in Asians</td>
<td>Higher incidence and severity of side effects in Asians</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Japanese vs. American</td>
<td>Greater in Japanese</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>BENZODIAZEPINES</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alprazolam</td>
<td>Asians vs. Caucasians</td>
<td>Lower for Asians</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>ANTIPSYCHOTICS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>Korean Americans vs. Caucasians</td>
<td>N/A</td>
<td>Clinically adjusted dose is lower in Koreans, and Koreans have a higher rate of central nervous system side effects</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Asians (Chinese, Japanese, Filipino, Korean, Vietnamese) vs. Caucasians</td>
<td>No difference</td>
<td>Effective dose and optimal response threshold are lower for Asians</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Chinese vs. non-Chinese (Caucasians, Hispanics, Blacks)</td>
<td>Higher mean blood levels in Chinese than in Americans (when given same dose)</td>
<td>Clinically adjusted dose is lower for Chinese than for non-Chinese</td>
</tr>
</tbody>
</table>

N/A, not available.
Racial differences in response to medications

As shown in Table 1, drugs used to treat conditions affecting the cardiovascular system and the central nervous system are frequently susceptible to the effects of genetic polymorphisms. Within the black population, the cardiovascular effects are especially notable.

High blood pressure is disproportionately prevalent in the black population and is associated with higher incidences of cerebrovascular and kidney complications and enlargement of the heart. However, the overall risk of coronary artery disease in the black male population is lower than that in white males, particularly in Europe and the Caribbean, and to a lesser extent in the U.S.

There are general differences in the underlying causes of high blood pressure between the black and white populations. For instance, black patients retain more salt and therefore have a higher incidence of salt-sensitive high blood pressure. These factors may underlie some of the observed differences in the effectiveness of various high blood pressure drugs in black populations. Ultimately, the choice of therapy must be tailored to the individual patient.

The Veterans Administration Cooperative Studies showed that blacks may respond differently to different beta-blockers. For example, the beta-blockers propranolol, nadolol, atenolol, and penbutolol were less effective among blacks than whites, but this differential effect can be eliminated by the addition of a diuretic. ACE inhibitors can be as effective in blacks as calcium channel blockers or diuretics, and in some cases they may be more effective as a first-line treatment. However, because lower doses of ACE inhibitors can be less effective in black patients, higher doses may be required than are normally prescribed. In patients with high blood pressure complicated by the presence of other medical conditions such as diabetes, ACE inhibitors are first-line agents in black as well as white patients. However, ACE inhibitors appear to be less effective in black populations for the prevention and treatment of heart failure in some patients.

Within Asian groups, central nervous system agents show similar susceptibility to genetic polymorphisms. In one study, lower dosages of antidepressants were found to be effective for Asians compared with Caucasians. Asians living in diverse areas of the world (Los Angeles, St. Louis, Hong Kong, and Beijing) have also shown consistently slower metabolism of tranquilizers, suggesting that genetic factors are more important than environmental factors in controlling the metabolism of these agents.

Tricyclic antidepressants have a narrow therapeutic index and therefore are among the most commonly affected central nervous system agents. Poor metabolizers and ultra-extensive metabolizers of these drugs may have clinical problems when they are taken at usually prescribed doses. Poor metabolizers often develop elevated blood concentrations, which may result in adverse effects. These side effects are rarely life threatening, but they are sufficiently unpleasant to cause problems with patient compliance. Ultra-extensive metabolizers, on the other hand, may not respond to recommended doses because drug concentrations are too low to be effective.

Hispanic patients have been reported to require lower doses of antidepressants and to experience more side effects compared with Caucasians.

Although there is a long-standing discussion about the best type of drug to use for treating high blood pressure in black patients, African Americans respond to drugs from all classes. There is no specific class of high blood pressure drugs that categorically should not be used based on race. Diuretics are frequently used to counteract increased salt retention among blacks. Although some studies find that beta-blockers, ACE inhibitors, and angiotensin receptor blocking agents do not control blood pressure in African Americans with the same degree of effectiveness as in whites, targeted blood pressure levels can usually be achieved by adding a second agent such as a low-dose diuretic.
of an antidepressant, African Americans achieved higher blood levels and faster therapeutic response, but also more side effects compared with whites. Ethn.

Ethnic groups such as Ashkenazi Jews may also respond differently to antipsychotic agents, especially with regard to side effects. A drug used to treat schizophrenia was associated with the development of a potentially life-threatening blood disorder in 20 percent of Jewish patients, although this adverse reaction develops in only about one percent of chronic schizophrenic patients in the general population. Genetic testing revealed that all of the affected Ashkenazi Jewish patients possessed a specific set of genes that is found in 83 percent of patients who developed the disease, but that these genes were found in only 8 percent of schizophrenic patients who did not develop the reaction. This set of genes occurs in 10 to 12 percent of the Jewish population in Israel and the U.S., but is characteristically found in less than one percent of the total Caucasian population of the U.S. The increased susceptibility of Ashkenazi Jews in this study to the development of this blood disorder as a result of drug therapy may be due to the more common presence of these genes among this ethnic group.

Medicines used to treat pain, such as codeine, can be influenced by genetic polymorphisms affecting central nervous system agents.

Cultural Factors

Cultural or psychosocial factors, such as the attitudes and health beliefs held by various groups, may affect the effectiveness of, or adherence to, a particular drug therapy. However, all persons from different ethnic and cultural groups share the universal need to be heard, to be respected, and to be valued. There also are some common cultural themes shared by all of the major ethnic groups. These themes can be organized into issues of trust and respect, health beliefs and practices, and family values. Although clearly not confined to a particular population, some specific themes may be more characteristic of some cultural groups than others.

Trust and respect

Sensitivity, understanding, and respect are essential to building trust. Trust is a vital determinant of treatment adherence and, ultimately, may be more important to therapeutic outcome than any procedure or medication. Trust is generated within the context of doctor-patient interactions, as illustrated below:

- Some cultural groups place great reliance on eye contact, body posture, and other non-verbal communications (facial expressions, nods of the head, tone of voice). When there is a language barrier, such body language assumes even greater importance.
- Physical contact is important to some patients who may feel slighted if the doctor does not touch them. To others, some physical touching may represent a cultural taboo particularly when related to gender differences.
Folk religion and healing rituals can be an important influence in the culture of working class immigrants, and a negative response to these rituals from the physician may be construed as a direct assault on their beliefs or religion. For example, newly arrived Hispanic immigrants in East Harlem often favor folk medicine and midwives, the type of health care familiar to them in the rural areas of their homeland, because they believe that medicine prescribed by an American health care provider is made of harmful chemicals and is therefore toxic. An example of this is an eight-year-old girl with AIDS who is prescribed several medications. "Although the purpose and side effects of each medication have been explained to her grandmother, she continues to use herbal remedies for her granddaughter’s affliction instead."

Another study of the use of folk healing and healers by Latinos from Columbia, the Dominican Republic and Guatemala living in New England found that “a major reason for not using mainstream health care providers more frequently was the perceived lack of holistic care and the use of medicines that are not natural.” Family nurse practitioners working with Mexican-Americans report that some of their clients are skeptical of Western medicine and only seek it when self-treatment and folk-healing have been unsuccessful.

For patients accustomed to a more formal relationship with their providers, a casual appearance or attitude may be detrimental to the development of respect and trust.

Providers may exhibit discriminatory behaviors toward minority patients by not involving them in health education or preventative medicine programs, believing they lack the necessary skills or are otherwise unable to benefit. As a result, referrals to specialists such as nutritionists or diabetes educators are sometimes delayed until the disease is advanced.

Some groups have an inherent distrust of the American health care system. Newly arrived Latinos in East Harlem viewed health care workers as extensions of government agencies and feared deportation or other negative consequences. For people of African heritage, there is a fear of being poisoned: the Tuskegee Syphilis Study is often cited as validating perceptions of racism and mistreatment.

Health Beliefs and Practices

Although cultural beliefs should be accorded respect, misinformation or lack of information should also be addressed. Problems may occur when patients do not tell their physician that they are taking herbal remedies or are seeing an alternative medicine practitioner. For example, 38 percent of Native American patients in an urban health center consulted with a Native American healer, and patients rated their healer’s advice higher than their physician’s advice 61 percent of the time. Only 15 percent of those seeing healers disclosed this to their physician. In another study, 83 percent of older Latin patients who reported using an alternative therapy in the previous month did not tell their physicians.

Patients’ beliefs regarding the properties and effects of medications are of central importance in determining compliance with treatment regimens. The following are examples of the complex influence of health beliefs and practices:

Traditional healing is important among a variety of population groups, and a dual system of health care services often exists. In a study of diverse populations in a metropolitan area, folk medicine remedies were used in addition to, rather than in place of, formal biomedical health care. Although individuals from different populations often use traditional practitioners and treatments, mixed use of these health care alternatives appears to be the most common pattern. Most complementary and alternative medicine therapies are used by U.S. adults in conjunction with conventional medical services. The overall use of these therapies
was higher for white non-Hispanic persons (31 percent) than for Hispanic (20 percent) and black non-Hispanic persons (24 percent).86

- Attitudes toward diet, exercise, smoking, drinking, and body image are imbedded in all cultural beliefs and practices, and these attitudes affect health and interactions with providers in important ways.

- Among some culturally-based attitudes is the belief that people should keep their illnesses to themselves. Persons holding such beliefs may be likely to seek treatment at later stages of the disease.

- The belief in fatalism exists among some populations, which can influence attitudes toward chronic disease. Even among young children, an attitude of passive acceptance is common. A fatalistic attitude impedes a direct confrontation with the consequences of unhealthy behaviors such as smoking.

- Among a group of older individuals in California, it was found that in contrast to African Americans, Latinos did not hold mainstream Western views about health and the management of illness.87 In fact, many Latinos appeared not to understand the meaning of “chronic” relating to illness, or their role in managing their illness beyond taking medication. They knew they must take their medication, but usually the disappearance of symptoms as a result of the medication was taken to be a cure. Each new episode was seen as a separate illness unrelated to previous episodes, particularly in illnesses with multiple symptoms. In addition, Mexican and Puerto Rican patients were found to be concerned about the addictive and toxic effects of medication, and thus reluctant to take medications indefinitely.88,89

- Immigrant minority groups may have access to controlled substances and other medications not generally available in the U.S. For example, antibiotic, neuroleptic, anti-emetic, and most other prescription drugs are easily obtained over the counter in Brazilian pharmacies, and many pain-relieving medicines are available without a prescription. Once in the U.S., it becomes difficult to obtain these drugs and persons requiring them on a regular basis often request friends to bring a supply from Brazil.90 In Haiti, many medications can be purchased without a prescription, so Haitians are often accustomed to keeping numerous topical and oral medicines on hand to treat various symptoms. For example, an individual who suspects a venereal disease may buy penicillin injections and have someone administer them without consulting a physician.90

Folk religion and healing rituals can be an important influence in the culture of working class immigrants, and a negative response to these rituals from the physician may be construed as a direct assault on their beliefs or religion.
Problems with Alternative Remedies

The use of alternative remedies and supplements is common. Among a multi-ethnic population, 10.4 percent were regular users of alternative medicines; 7.4 percent regularly used non-prescribed vitamin supplements; and 5.3 percent used cod liver oil, primrose oil, or garlic preparations. People of African origin were more likely to use alternative medicines than either whites or South Asians, who were the least common users.91

However the use of complementary and alternative medications can result in drug interactions, disease interactions, adverse reactions, or toxic effects:

- An evaluation of the use of alternative preparations in the El Paso, Texas region identified 599 instances of use of such remedies that could result in these effects, based on interviews with 547 survey participants.92
- A survey of Spanish-speaking Latino families visiting a pediatric clinic in Salt Lake City found that 39 percent of parents from Mexico and 21 percent from other countries reported using a nonsteroidal anti-inflammatory drug (metamizole) associated with a blood disorder side effect.93 The drug is available over-the-counter in Latin American countries and in markets serving immigrant communities in the U.S.
- Dozens of Chinese herbal remedies available in the U.S. contain the toxin aristolochic acid. The toxin was implicated in an outbreak of kidney trauma in Belgium, possibly causing cancers in more than 30 people, and is suspected of the same in several other countries.94 Another study found clinically relevant liver enzyme elevations in about 1 of 100 patients treated with traditional Chinese drugs.95

Family Values

The strengths of the African American, Asian, Hispanic, and Native American family values, along with extended family, church and community organizations, can be important resources in supporting the patient and in facilitating adherence to medication and other treatment regimens. Such networks can provide substantial support in times of illness.

- Opinions of Asian family members and other elders are accorded great respect in times of illness. In Hispanic families, the mother or grandmother (of the husband especially) usually makes the health care decisions. In addition, the needs of the children are always paramount. Health care providers need to be aware of these relationships to optimize adherence to treatment regimens.

- Family atmosphere may influence response to medications. Non-Western patients with schizophrenia were found to have more social support and better clinical outcomes than their Western counterparts. Patients whose family members expressed frequent criticism, hostility, and emotional over-involvement relapsed more frequently and required higher doses of medication.96,97

- Despite the wide use of a variety of non-Western treatments, the actual remedies may not be perceived to be as critical to care as the meaning of the cultural memories inherent in acts of caring. For example, within Puerto Rican and African American groups, comfort, nurturance, and familiarity were found to be “intrinsic to the holistic nature of the remedies used and to be salient features of the memories of healing and curing.”98

91. [Source]
92. [Source]
93. [Source]
94. [Source]
95. [Source]
96. [Source]
97. [Source]
98. [Source]
Effect of cultural factors on medication compliance

Patients’ beliefs regarding the properties and effects of medications are of central importance in determining compliance. For instance, some patients from non-Western backgrounds are unfamiliar with the practice of taking long-term medication for chronic illness and with the notion of accepting unpleasant side effects as the price for effective treatment. These reasons may account for why some patients stop taking their medication. Variations in attitudes toward medicines tend to be driven by national characteristics, culture, and philosophy. Immigrants from countries with different non-Western medical cultures may therefore have different expectations regarding the type of drug prescribed, tolerance of side effects, dosage form preference, or other aspects of drug therapy. This clash between patient and provider expectations may result in noncompliance with medications.

In comparison to other societies, American medicine tends to be very aggressive, leading to a greater focus on the effectiveness of treatment and a greater tolerance of side effects. Downward dosage adjustment by Asian patients is common and results from the perception that Western medicines are too strong and that even relatively benign side effects are intolerable.

In Japan, in general, a medicine’s safety profile is stressed more than its effectiveness. This “pharmaceutical conservatism” mirrors the Japanese focus on slow and careful building of personal relationships and consensus-based business decisions. This emphasis on safety and a systematic approach may explain, in part, the general use of lower dosages compared with dosages used in the West, and the lower incidence of side effects reported by Japanese compared with American and European patients. In addition, patients in Japan frequently are treated with multiple medications because Asian patients often believe that multiple drugs are more effective than monotherapy since multiple herbal ingredients are usually prescribed by traditional Asian doctors.

European medicine reflects a middle-position between the poles of American and Japanese medical cultures. European practices differ in terms of the patterns and types of drugs prescribed, the preference for different dosage forms (the French favor suppositories, Latin Americans expect injections), and diagnoses in some countries that are not used in others (see for a detailed discussion).

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**Downward dosage adjustment by Asian patients is common and results from the perception that Western medicines are too strong and that even relatively benign side effects are intolerable.**

There is also a general expectation among many cultures that medicines will provide quick relief from symptoms, and thus do not need to be taken long-term. In some developing countries, medications are customarily prescribed for only a day or two. These beliefs may reflect their experiences with indigenous herbal preparations, which generally cause fewer side effects, and with analgesics and antibiotics, which work rapidly. Hispanics and Asians often expect rapid results and are cautious about the side effects of Western medicines. These beliefs may interfere with the acceptance of drugs with a delayed onset of action (e.g., antidepressants).

Lastly, poor health literacy may negatively impact patients’ ability to take medications properly. Members of groups for whom English is a second language are more likely than socioeconomically advantaged white adults to have limited literacy skills, and there is a relationship between low literacy and self-management skills, including taking medications properly.

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**Some patients are unfamiliar with the Western practice of taking long-term medication for chronic illness and with the notion of accepting unpleasant side effects as the price for effective treatment.**
Technological advances in the 1990s have changed the nature of pharmacogenetic research and its future impact on medicine. In the early decades of its existence, pharmacogenetics focused on the enzymes responsible for drug metabolism. Differences in the genes encoding these enzymes were inferred from differences in the structure and activity of the enzymes themselves. The frequencies of polymorphisms in drug metabolism enzymes were observed to vary among different populations defined on the basis of race. Thus, race is one factor (among many) that changes the probability that an individual person will respond to a given drug.

Two features of the genomics revolution, with the Human Genome Project as its centerpiece, have important consequences for the relationship between drug therapy and race. First, genetic variations are now determined by direct analysis of genes themselves. Gene sequencing (i.e., determination of a gene’s nucleotide sequences) has become a rapid and automated process. Second, the entire spectrum of genes that determine drug behavior and sensitivity now can be studied genetically. That is, the effect of the entire genome on drug behavior can be determined rather than the effect of the individual gene – hence the change from pharmacogenetics to pharmacogenomics.

In the future, drug treatment will be individually tailored rather than based on race or other categories such as sex or age. However, the full impact of these changes will take many years to unfold. Genetic fingerprinting using DNA arrays is already practical, but the knowledge base relating genomic variations to drug response and disease progression has not been developed. Observational studies are under way in which DNA fingerprints are being correlated with data present in medical records about medical history and drug response, and it is expected that the medical records of an entire country (Iceland) will be correlated with genomic data. These developments will surely have a profound impact on the ways in which new drugs are developed and used.

Continuing research in pharmacogenomics is likely to reveal significant and far-ranging information regarding inter-individual and cross-racial differences in the actions of new and existing drugs.

Continuing research in pharmacogenomics is likely to reveal significant and far-ranging information regarding inter-individual and cross-racial differences in the actions of new and existing drugs. These developments, along with the increasing prevalence and influence of patients from a variety of races and ethnicities and the continued pressure to manage health care costs, will require programs having the dual objectives of cost control and individualized therapy for a racially and ethnically diverse population of Americans. Balancing these objectives will challenge health policy makers in the coming decades.
As a result of advances in pharmacogenetics research, as well as political and social changes affecting racial and ethnic groups, more consideration is being given to the need for individualized drug therapy. The availability of a broad range of medicines enables physicians to treat patients with precision and provides options when the first agent used is ineffective, not tolerated, or proper compliance is not achievable. Often, one drug cannot simply be substituted for another of the same class because its clinical effects may vary among racial and ethnic groups due to differences in drug metabolism. In order for health care practitioners to engage in racially and ethnically appropriate prescribing, a wide range of options must therefore remain available.

Policies that arbitrarily limit drug choices stand in opposition to an increasing body of evidence indicating that drug therapy does the most good (and the least harm) when it is tailored to the individual. Individualized prescribing takes into account a number of factors, among them environmental, genetic, and cultural factors that may affect a drug’s effectiveness and compliance with prescribed treatment regimens.

These factors are relevant to the implementation of pharmaceutical cost management policies. Such policies must consider any possible discriminatory effects on racial and ethnic groups. Limiting access to optimal medications may produce reduced or unexpected responses in subpopulations. Access to a variety of medications and dosing formulations, especially those enabling simplified administration (e.g., once-daily or without regard to food) can facilitate compliance and may be particularly beneficial for patients with low health literacy who may have trouble following complex instructions. Additionally, patients with low health literacy or language barriers may be ill-equipped to understand the limitations of restrictive policies and the appeals processes necessary to obtain a more appropriate drug. Restricting access to medications that will provide optimal care can contribute to existing disparities in health care.

The following recommendations offer practical suggestions that could not only benefit the quality of care provided by health care institutions and physicians, but could also be useful in controlling health care costs.

1. **Health care institutions should implement pharmaceutical cost containment practices that are broad and flexible enough to enable rational choices of drugs and formulations for all patients, regardless of race or ethnic origin.**

2. **Pharmaceutical companies should continue to include significant numbers of patients from varied racial and ethnic backgrounds in drug metabolism and clinical trials in cases where genetic polymorphism for that drug class is relevant.** The vast majority of drug manufacturers test and evaluate new pharmacological compounds on population subgroups, including racial and ethnic subgroups. This is likely to reveal drug actions and side effects specific to these groups, and may lead to the discovery of therapies of specific advantage to these populations. It may also reveal cultural barriers to use of the drug among particular groups.

3. **Hospitals, managed care groups, and other providers of health care services should endeavor to employ practitioners who are racially and ethnically representative of the patient population being served.** There is, however, a short supply of physicians from backgrounds representing our most important minority groups. Given this dearth of providers, we must seek to train the existing health care professionals to provide appropriate care to culturally diverse clients. Provider organizations should develop and institute specific training for all practitioners who have direct patient contact – especially physicians, pharmacists, nurses, and physician assistants.

4. **Health care providers should give individualized treatment to each patient.** For the practicing physician, each patient represents a unique and dynamic interaction among several determinants including environmental, genetic, and cultural. Although it may be impossible for a physician to anticipate how a particular patient will respond in every instance, it is imperative to individualize therapy with respect to the appropriate choice of both drug and dose, and to make sure that the patient both
understands and is able and willing to comply with the prescribed treatment.

5. Physicians should be alert to atypical drug responses or unexpected side effects when they treat patients from varied racial and ethnic backgrounds. Patients may not be taking the medication properly due to misunderstood instructions, or misperceptions of Western medicine or the severity of disease. Dosage adjustments may need to be made for patients from different groups as supported by pharmacological evidence.

6. Providers should take special care to communicate clearly and concisely with patients for whom there may be a linguistic communications barrier or a concern about the patient’s level of health literacy. This also involves perceiving and surmounting less visible barriers such as patient confidence, shame, or fear. Practitioners must be able to communicate effectively across cultural, socioeconomic, educational, and geographical differences. Any written materials distributed should be appropriate to the patient’s level of health literacy and should reinforce spoken dialogue.

7. Because advances in pharmacogenomics will improve the ability to individualize treatment, all who are involved in patient care should actively monitor developments in this area to take advantage of new diagnostic and therapeutic technologies as they become available.
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