linear function best described the data (Burnett et al. 1997a,b; Jaffe et al. 2003; Tenias et al., 1998; Castellsague et al., 1995). These results do not provide adequate evidence to suggest that nonlinear departures exist along any part of this range of NO₂ exposure concentrations. Evidence from human clinical studies has not helped to clarify understanding of the concentration-response function of NO₂ (see chapter 3).

4.3. Susceptible and Vulnerable Populations

The NAAQS are intended to provide an adequate margin of safety for both general populations and sensitive subpopulations, or those subgroups potentially at increased risk for ambient air pollution health effects. The term susceptibility generally encompasses innate or acquired factors that make individuals more likely to experience effects with exposure to pollutants. Genetic or developmental factors can lead to innate susceptibility, while acquired susceptibility may result from age, disease, or personal risk factors such as smoking, diet, or exercise. In addition, new attention has been paid to the concept of some population groups having increased vulnerability to pollution-related effects due to extrinsic factors including socioeconomic status (e.g., reduced access to health care) or particularly elevated exposure levels. Potentially susceptible and/or vulnerable groups comprise a large fraction of the U.S. population. Given the likely heterogeneity of individual responses to air pollution, the severity of health effects experienced by a susceptible subgroup may be much greater than that experienced by the population at large (Zanobetti et al., 2000).

Many factors such as genetic (Kleeberger et al., 2005) and social (Gee and Payne-Sturges, 2006) determinants of disease may contribute to interindividual variability and heightened susceptibility to NO₂. The previous NOₓ AQCD (U.S. Environmental Protection Agency, 1993) identified certain groups within the population that may be more susceptible to the effects of NO₂ exposure, including persons with preexisting respiratory disease, children, and older adults. Findings from recent studies supported the conclusions from the previous assessment with regard to susceptibility.

4.3.1. Preexisting Disease as a Potential Risk Factor

A recent report of the National Research Council (NRC) emphasized the need to evaluate the effect of air pollution on susceptible groups including those with respiratory illnesses and cardiovascular disease (CVD) (NRC, 2004). Generally, chronic obstructive pulmonary disease (COPD), conduction disorders, CHF, diabetes, and MI are conditions believed to put persons at greater risk for adverse events associated with air pollution. In addition, epidemiologic evidence indicates persons with airway hyperresponsiveness as determined by methacholine provocation may be at greater risk for symptoms such as phlegm and lower respiratory symptoms than subjects without airway hyperresponsiveness (Boezen et al., 1998). Several researchers have investigated the effect of air pollution among potentially sensitive groups with preexisting medical conditions.

4.3.1.1. Asthmatics

Evidence from epidemiologic studies shows an association between NO₂ exposure and children’s hospital admissions, ED visits, and calls to doctors for asthma. This evidence came from large longitudinal studies, panel studies, and time-series studies. NO₂ exposure was associated with aggravation of asthma effects that include symptoms, medication use, and lung function. Effects of NO₂ on asthma were most evident with a cumulative lag of 2 to 6 days, rather than same-day levels of NO₂. Time-series studies also demonstrated a relationship in children between hospital admissions or ED visits for asthma
and NO₂ exposure, even after adjusting for copollutants such as PM and CO. Important evidence was also available from epidemiologic studies of indoor NO₂ exposures. A number of recent studies showed associations with wheeze, chest tightness, and length of symptoms (Belanger et al., 2006); respiratory symptom rates (Nitschke et al., 2006); school absences (Pilotto et al., 1997a); respiratory symptoms, likelihood of chest tightness, and asthma attacks (Smith et al., 2000); and severity of virus-induced asthma (Chauhan et al., 2003). However, several studies (Mukala et al., 1999, 2000; Farrow et al., 1997) evaluating younger children found no association between indoor NO₂ and respiratory symptoms.

Airway hyperresponsiveness in asthmatics to both nonspecific chemical and physical stimuli and to specific allergens appeared to be the most sensitive indicator of response to NO₂ (U.S. Environmental Protection Agency, 1993). Responsiveness is determined using a challenge agent, which causes an abnormal degree of constriction of the airways as a result of smooth muscle contraction. This response ranges from mild to severe (spanning orders of magnitude) and is often accompanied by production of sputum, cough, wheezing, shortness of breath, and chest tightness. Though some asthmatics do not have this bronchoconstrictor response (Pattemore et al., 1990), increased airway hyperresponsiveness is correlated with asthma symptoms and increased asthma medication usage. Clinical studies reported increased airway hyperresponsiveness to allergen challenge in asthmatics following exposure to 0.26-ppm NO₂ for 30 min during rest (Barck et al., 2002; et al.; Strand et al., 1997; 1998).

Toxicological studies provided biological plausibility that asthmatics are likely susceptible to the effects of NO₂ exposure. Numerous animal studies provide evidence that NO₂ can produce inflammation and lung permeability changes. These studies provided evidence for several mechanisms by which NO₂ exposure can induce effects, including reduced mucociliary clearance, and alveolar macrophage function such as depressed phagocytic activity and altered humoral- and cell-mediated immunity. Chauhan et al. (2003) reviewed potential mechanisms by which NO₂ exacerbates asthma in the presence of viral infections. These mechanisms included “direct effects on the upper and lower airway by ciliary dyskinesia, epithelial damage, increases in pro-inflammatory mediators and cytokines, rises in IgE concentration, and interactions with allergens, or indirectly through impairment of bronchial immunity.” These are all mechanisms that can provide biological plausibility for the NO₂ effects in asthmatic children observed in epidemiologic studies. However, it must be noted that the experimental animal studies that looked at effects on markers of inflammation, such as BAL fluid levels of total protein and lactate dehydrogenase and recruitment or proliferation of leukocytes, occurred only at exposure levels of ≥ 5 ppm. Studies conducted at these higher exposure concentrations may elicit mechanisms of action and effects that do not occur at near-ambient levels of NO₂.

### 4.3.1.2. Cardiopulmonary Disease and Diabetes

While less evidence was available for these conditions, preexisting cardiovascular-related conditions may lead to heightened susceptibility to the effects of NO₂ exposure. Recent epidemiologic studies reported that persons with preexisting conditions may be at increased risk for adverse cardiac health events associated with ambient NO₂ concentrations (Peel et al., 2007; Mann et al., 2002; D’Ippoliti et al., 2003; von Klaut et al., 2005). Peel et al. (2007) reported evidence of effect modification by comorbid hypertension and diabetes on the association between ED visits for arrhythmia and NO₂ exposure. In another study, a statistically significant positive relationship was reported between NO₂ concentrations and hospitalizations for IHD among those with prior diagnoses of CHF and arrhythmia (Mann et al., 2002). However, Mann et al. (2002) noted the vulnerability in the secondary CHF group could be due to increased prevalence of MI as the primary diagnosis in this group. In addition, these authors stated they were unable to distinguish the effects of NO₂ from other traffic pollutants (Mann et al., 2002). Von Klaut et al. (2005) reported cardiac readmission among MI survivors was associated with NO₂ and this association was robust to adjustment for PM₁₀. Modification of the association between NO₂ and MI by conduction disorders but not diabetes or hypertension was observed by D’Ippoliti et al. (2003).
Park et al. (2005b) examined the relationship of NO$_2$ and HRV among those with IHD, hypertension and diabetes but did not find an association.

There was limited evidence from clinical or toxicological studies on potential susceptibility to NO$_2$ in persons with CVD; however, the limited epidemiologic evidence indicated that these individuals may be more sensitive to effects of NO$_2$ exposure or air pollution in general. Reductions in blood hemoglobin (~10%) have been reported in healthy subjects following exposure to NO$_2$ (1 to 2 ppm) for a few hours during intermittent exercise (Frampton et al., 2002). The clinical importance of hemoglobin reduction in persons with significant underlying lung disease, heart disease, or anemia has not been evaluated, but the reductions could lead to adverse cardiovascular consequences. These consequences would be exacerbated by concomitant exposure to CO, a combustion copollutant of NO$_2$ that binds to hemoglobin and reduces oxygen availability to tissues and organs.

### 4.3.2. Age as a Potential Risk Factor

Children and older adults (65+ years) are often considered at increased risk from air pollution compared to the general population. The American Academy of Pediatrics (2004) concluded that children and infants are among the most susceptible to many air pollutants, including NO$_2$. Because 80% of alveoli are formed postnatally and changes in the lung continue through adolescence, the developing lung is highly susceptible to damage from exposure to environmental toxicants (Dietert et al., 2000). In addition to children, older adults frequently are classified as being particularly susceptible to air pollution. The basis of the increased sensitivity in the elderly is not known, but one hypothesis is that it may be related to changes in the respiratory tract lining’s fluid antioxidant defense network and/or to a decline in immune system surveillance or response (Kelly et al., 2003). The generally declining health status of many older adults may also increase their risks to air pollution-induced effects.

Evidence showed that associations of NO$_2$ with both respiratory ED visits and hospitalizations were stronger among children (Peel et al., 2005; Atkinson et al., 1999b; Fusco et al., 2001; Hinwood et al., 2006; Anderson et al., 1998) and older adults (Migliaretti et al., 2005; Atkinson et al., 1999b; Schouten et al., 1996; Ponce de Leon et al., 1996; Prescott et al., 1998). However, two studies (Sunyer et al., 1997; Migliaretti et al., 2005) found no difference in the rates of ED visits associated with NO$_2$ concentrations for children (<15 years) and adults (15 to 64 years). Luginaah et al. (2005) and Wong et al. (1999) found no statistically significant difference in the elderly and adult age groups.

Many field studies focused on the effect of NO$_2$ on the respiratory health of children, while fewer field studies have compared the effect of NO$_2$ in adults and other age groups. In general, children and adults experienced decrements in lung function associated with short-term ambient NO$_2$ exposures (see Section 3.1.5). Importantly, a number of long-term exposure studies indicated that effects in children that include impaired lung function growth, increased respiratory symptoms and infections, and onset of asthma (see Section 3.4).

In elderly populations, associations between NO$_2$ and hospitalizations or ED visits for CVD, including stroke, have been observed in several studies (Anderson et al., 2007a; Atkinson et al., 1999b; Jalaludin et al., 2006; Hinwood et al., 2005; Wong et al., 1999; Barnett et al., 2006; Zanobetti and Schwartz, 2006; Simpson et al., 2005a; Wellenius et al., 2005b; Morgan et al., 1998a; Morris et al., 1995). However, some results were inconsistent across cities (Morris et al., 1995), and investigators could not distinguish the effect of NO$_2$ from the effect of other traffic-related pollutants such as PM and CO (Simpson et al., 2005a; Barnett et al., 2006; Morgan et al., 1998b; Jalaludin et al., 2006; Zanobetti and Schwartz, 2006).

Several mortality studies investigated age-related differences in NO$_2$ effects. Among the studies that observed positive associations between NO$_2$ and mortality, a comparison of all-age– or ≤ 64-years-of-age–group NO$_2$–mortality risk estimates to that of the > 65-years-of-age group indicated that, in general, the elderly population was more susceptible to NO$_2$ effects (Biggeri et al., 2005; Burnett et al.,
2004). One study (Simpson et al., 2005a) found no difference in increases in CVD mortality associated with NO₂ concentrations between all ages and those participants of ≥ 65 years of age.

### 4.3.3. Gender as a Potential Risk Factor

A limited number of studies stratified results by gender. Lugeninaah et al. (2005) found increases in hospital admissions associated with NO₂ among females but not males. In a study of children in Toronto, Canada, NO₂ was positively associated with asthma admissions among both boys and girls (Lin et al., 2005). However, in a study of asthma admissions among children in Vancouver, NO₂ was significantly and positively associated with asthma hospitalization only for boys in the low socioeconomic group (Lin et al., 2004). An increased association with asthma with exposure to traffic pollutants was observed for girls (Kim et al., 2004a). Decrements in FVC and FEV₁ growth associated with NO₂ were reported in male and female children in Mexico (Rojas-Martinez et al., 2007a, b).

### 4.3.4. Genetic Factors for Oxidant and Inflammatory Damage

A consensus now exists among epidemiologists that genetic factors related to health outcomes and ambient pollutant exposures merit serious consideration (Kauffmann et al., 2004; Gilliland et al., 1999; ATS 2000b). Interindividual variation in human responses to air pollutants may indicate that that some subpopulations are at increased risk of detrimental effects from pollutant exposure, and it has become clear that genetic background is an important susceptibility factor (Kleeberger, 2005). Several criteria must be satisfied in selecting and establishing useful links between polymorphisms in candidate genes and adverse respiratory effects. First, the product of the candidate gene must be instrumentally involved in the pathogenesis of the adverse effect of interest, often a complex trait with many determinants. Second, polymorphisms in the gene must produce a functional change in either the protein product or in the level of expression of the protein. Third, in epidemiologic studies, the issue of confounding by other environmental exposures must be carefully considered. In general, work has focused on genes involved in oxidant and inflammation damage.

Several glutathione S-transferase (GST) genes have common, functionally important polymorphic alleles that affect host defense function in the lung (e.g., homozygosity for the null allele at the GSTM1 and GSTT1 loci, homozygosity for the A105G allele at the GSTP1 locus). GST genes are inducible by oxidative stress. Exposure to radicals and oxidants in air pollution induces decreased GSH that increases transcription of GSTs. Individuals with genotypes that result in enzymes with reduced or absent peroxide activity are likely to have reduced oxidant defenses and potentially increased susceptibility to inhaled oxidants and radicals.

Studies of genotype, respiratory health, and air pollution in general have been conducted (Lee et al., 2004; Gilliland et al., 2002; Gauderman et al., 2007). NO₂-related genetic effects have been presented primarily by Romieu et al. (2006) and indicated that asthmatic children with GSTM1 null and GSTP1 Val/Val genotypes appear to be more susceptible to developing respiratory symptoms related to O₃, but not NO₂, concentrations. Though, it was hypothesized that ambient NO₂ concentrations may affect breathing in general in children regardless of their GSTM1 or GSTP1 genotypes, GSTM1-positive and GSTP1 Ile/Ile- and Ile/Val-genotype children were more likely to experience cough and bronchodilator use, specifically in response to NO₂ than GSTM1-null and GSTP1-Val/Val children. Contrary to expectations, a 20-ppb increase in ambient NO₂ concentrations was associated with a decrease in bronchodilator use among GSTP1 Val/Val-genotype children. It remains plausible that there are genetic factors that can influence health responses to NO₂, though the few available studies did not provide specific support for genetic susceptibility to NO₂ exposure.
4.3.5. Other Potentially Susceptible Populations

Although data specific to NO2 exposures was lacking for many of the susceptibility factors listed below, several potentially susceptible groups deserve specific mention in this document. These include individuals in a chronic pro-inflammatory state (e.g., diabetics), obesity, and children born prematurely or with low birth weight.

Factors that may influence susceptibility or vulnerability are:

Susceptibility Factors
- Age, Gender
- Adverse birth outcomes: e.g., preterm birth, low birth weight, growth restriction, birth defects
- Race/ethnicity
- Genetic factors
- Pre-existing disease, e.g., diabetes
- Obesity
- Respiratory diseases, e.g., asthma, COPD
- Cardiovascular diseases

Vulnerability Factors
- Socioeconomic status
- Education level
- Air conditioning Use
- Proximity to Roadways
- Geographic Location (West vs. East)
- Level of Exercise
- Work Environment (e.g., outdoor workers)

Chronic inflammation appears to enhance susceptibility for air pollution-related cardiovascular events in older individuals and persons with diabetes, coronary artery disease, obesity, and past myocardial infarctions (Bateson and Schwartz 2004, Goldberg et al., 2001; Zanobetti and Schwartz, 2002; Peel et al. 2007). Dubowsky et al. (2006) reported that individuals with conditions associated with both chronic inflammation and increased cardiac risk were more vulnerable to the short-term pro-inflammatory effects of air pollution. This included individuals with diabetes, obesity, and concurrent diabetes, obesity and hypertension. Zanobetti and Schwartz (2001) reported more than twice the risk for hospital admissions for heart disease in persons with diabetes than in persons without diabetes associated with exposure to ambient air pollution, indicating that persons with diabetes are an important at-risk group. Data from the Third National Health and Nutrition Examination Survey indicated that 5.1% of the U.S. population older than 20 years of age has diagnosed diabetes and an additional 2.7% has undiagnosed diabetes (Harris et al., 1998). Moreover, another study found that subjects with impaired glucose tolerance without type II diabetes also had reduced HRV (Schwartz, 2001). This may indicate that the at-risk population may be even larger.

Mortimer et al. (2000) reported that among asthmatic children, birth characteristics continue to be associated with increased susceptibility to air pollution later in life, demonstrating that air pollution-induced asthma symptoms were more severe in children born prematurely or of low birth weight. Specifically, the authors revealed asthmatic children born more than three weeks prematurely or weighing less than 2,500 grams (5.5 pounds) had a six-fold decrease in breathing capacity associated with air pollution compared to full-weight, full-term children. The low birth weight and premature children also reported a five-fold greater incidence of symptoms like wheezing, coughing and tightness in the chest.

4.3.6. Increased Vulnerability Associated with Increased Exposure

Certain groups may experience relatively high exposure to NO2, thus forming a potentially vulnerable population. Many studies found that indoor, personal, and outdoor NO2 levels are strongly
associated with proximity to traffic or traffic density (see Section 2.5.4). NO$_2$ concentrations in heavy traffic or on freeways, have been observed in the range of 40 to 70 ppb and can be more than twice the residential outdoor or residential/arterial road level (Lee et al., 2000; Westerdahl et al., 2005). Due to high air exchange rates, NO$_2$ concentrations inside a vehicle could rapidly approach levels outside the vehicle during commuting; the mean in-vehicle NO$_2$ concentration has been observed to be between 2 to 3 times non-traffic ambient levels (see Section 2.5.4). Those with occupations that require them to be in or close to traffic or roadways (e.g., bus and taxi drivers, highway patrol officers, toll collectors) or those with long commutes could be exposed to relatively high levels of NO$_2$ compared to ambient levels.

SES is a known determinant of health, and there is evidence that SES modifies the effects of air pollution (O’Neill et al. 2003; Makri and Stilianakis, 2008). Higher exposures to air pollution and greater susceptibility to its effects may contribute to a complex pattern of risk among those with lower SES. Conceptual frameworks have been proposed to explain the relationship between SES, susceptibility, and exposure to air pollution. Common to these frameworks is the consideration of the broader social context in which persons live, and its effect on health in general (O’Neill et al., 2003; Gee and Payne-Sturges, 2004), as well as on maternal and child health (Morello-Frosch and Shenassa, 2006) and asthma (Wright and Subramanian, 2007) specifically. Multilevel modeling approaches that allow parameterization of community-level stressors such as increased life stress as well as individual risk factors were considered by these authors. In addition, statistical methods that allow for temporal and spatial variability in exposure and susceptibility have been discussed in the recent literature (Jerrett and Finkelstein, 2005; Künzli et al., 2005).

Many recent studies examined modification by SES indicators on the association between mortality and PM (O’Neill et al., 2003; Martins et al., 2004; Jerrett et al., 2004; Finkelstein et al., 2003; Romieu et al., 2004a) or other indices such as traffic density, distance to roadway or a general air pollution index (Ponce et al., 2005; Woodruff et al., 2003; Finkelstein et al., 2004). SES modification of NO$_2$ associations has been examined in fewer studies. For example, in a study conducted in Seoul, Korea, community-level SES indicators modified the association of air pollution with ED visits for asthma; of the five criteria air pollutants evaluated, NO$_2$ showed the strongest association in lower SES districts compared to high SES districts (Kim et al., 2007.) In addition, Clougherty et al. (2007) evaluated exposure to violence (a chronic stressor) as a modifier of the effect of traffic-related air pollutants, including NO$_2$, on childhood asthma. The authors reported an elevated risk of asthma with a 4.3-ppb increase in NO$_2$ exposure solely among children with above-median exposure to violence in their neighborhoods.

### 4.4. At-Risk Susceptible Population Estimates

Although NO$_2$-related health risk estimates may appear to be small, they may well be important from an overall public health perspective owing to the large numbers of persons in the potential risk groups. Several population groups have been identified as possibly having increased susceptibility or vulnerability to adverse health effects from NO$_2$, including children, older adults, and persons with preexisting pulmonary diseases. One consideration in the assessment of potential public health impacts is the size of various population groups that may be at increased risk for health effects associated with NO$_2$-related air pollution exposure. Table 4.4.1 summarizes information on the prevalence of chronic respiratory conditions in the U.S. population in 2004 and 2005 (National Center for Health Statistics, 2006a,b). Individuals with preexisting cardiopulmonary disease constitute a fairly large proportion of the population, with tens of millions of persons included in each disease category. Of most concern are those persons with preexisting respiratory conditions, with approximately 10% of adults and 13% of children having been diagnosed with asthma and 6% of adults with COPD (chronic bronchitis and/or emphysema).

There are approximately 2.5 million deaths from all causes per year in the U.S. population, with about 100,000 deaths from chronic lower respiratory diseases (Kochanek et al., 2004) and 4,000 from
asthma (NCHS, 2006c). For respiratory health diseases, there are nearly 4 million hospital discharges per year (DeFrances et al., 2005), 14 million ED visits (McCaig and Burt, 2005), 112 million ambulatory care visits (Woodwell and Cherry, 2004), and an estimated 700 million restricted-activity days per year due to respiratory conditions (Adams et al., 1999). Of the total number of visits for respiratory disease, 1.8 million annual ED visits were reported for asthma, including more than 750,000 visits by children. In addition, nearly 500,000 annual hospitalizations for asthma were reported (NCHS, 2006c).

Centers for Disease Control and Prevention (CDC) analyses have shown that the burden of asthma has increased over the past two decades (NCHS, 2006c). In 2005, approximately 22.2 million people (7.7% of the population) had asthma. The incidence was higher among children (8.9% of children) compared to adults (7.2%) (Note: 2004 data is shown in Table 4.4-1, with a prevalence of 6.7%). In addition, prevalence and severity is higher among certain ethnic or racial groups such as Puerto Ricans, American Indians, Alaskan Natives, and African Americans. The asthma hospitalization rate for black persons was 240% higher than for white persons. Puerto Ricans were reported to have the highest asthma death rate (360% higher than non-Hispanic white persons) and non-Hispanic black persons had an asthma death rate that was 200% higher than non-Hispanic white persons. Furthermore, a higher prevalence of asthma among persons of lower SES and an excess burden of asthma hospitalizations and mortality in minority and inner-city communities have been observed in several studies (Wright and Subramanian, 2007). Gender and age are also determinants of prevalence and severity: adult females had a 40% higher prevalence than adult males; and boys, a 30% higher prevalence than girls. Overall, females had a hospitalization rate about 35% higher than males.

<table>
<thead>
<tr>
<th>CHRONIC CONDITION/DISEASE</th>
<th>AGE (YEARS)</th>
<th>REGION</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL ADULTS</td>
<td>18-44</td>
<td>45-64</td>
</tr>
<tr>
<td>Asthma</td>
<td>14.4</td>
<td>6.7</td>
</tr>
<tr>
<td>COPD: Chronic Bronchitis</td>
<td>8.6</td>
<td>4.2</td>
</tr>
<tr>
<td>COPD: Emphysema</td>
<td>3.5</td>
<td>1.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CHRONIC CONDITION/DISEASE</th>
<th>ALL CHILDREN</th>
<th>0-4</th>
<th>5-11</th>
<th>12-17</th>
<th>NORTH-EAST</th>
<th>MID-WEST</th>
<th>SOUTH</th>
<th>WEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Conditions</td>
<td>6.5</td>
<td>8.9</td>
<td>6.8</td>
<td>9.9</td>
<td>9.6</td>
<td>10.1</td>
<td>8.5</td>
<td>9.3</td>
</tr>
</tbody>
</table>

Source: National Center for Health Statistics (2006a,b)

In addition, population groups based on age group also comprise substantial segments of the population that may be potentially at risk for NO2-related health impacts. Based on U.S. census data from 2000, about 72.3 million (26%) of the U.S. population are under 18 years of age, 18.3 million (7.4%) are under 5 years of age, and 35 million (12%) are 65 years of age or older. Hence, large proportions of the U.S. population are in age groups that are likely to have increased susceptibility and vulnerability for health effects from ambient NO2 exposure.
Based on data from the American Housing Survey, approximately 36 million persons live within 300 feet (~90 meters) of a four-lane highway, railroad, or airport and 12.6% of U.S. housing units are located within this distance (U.S. Census Bureau, 2006). Furthermore, several exposure studies offer insight into differential exposures to NO₂ from traffic in childhood. In California, 2.3% of schools, grades K–12, with a total enrollment of more than 150,000 students were located within ~500 feet (150 m) of high-traffic roads, and a higher proportion of nonwhite and economically disadvantaged students attended schools within close proximity to these high-traffic roadways (Green et al., 2004). Similar findings were reported for Detroit schoolchildren (Wu and Batterman, 2006). Figure 4.4-1 shows the proportion of study populations in Boston, MA (Garshick et al. 2003) and Los Angeles, CA (McConnell et al. 2006), the entire U.S. (American Housing Survey, 2005), and from population exposure models (HAPEM6, 2007) living within a certain distance from major roadways. It also presents results of air quality measurements showing the decrease in concentration of black carbon, a traffic-related pollutant, with increasing distance from the roadway. The considerable size of the population groups at risk indicate that exposure to ambient NO₂ could have an impact on public health in the U.S.
4.5. Summary of Public Health Issues

In the few studies that specifically examined concentration-response relationships between NO2 and health outcomes, there was little evidence of an effect threshold. However, various factors, such as interindividual variation in response, additivity to background of effect and/or exposure, and measurement error tend to linearize the concentration-response relationship and obscure any population-level thresholds that might exist.

Persons with preexisting respiratory disease, children, and older adults may be more susceptible to the effects of NO2 exposure. Individuals in sensitive groups may be affected by lower levels of NO2 than the general population or experience a greater impact with the same level of exposure. A number of factors may increase susceptibility to the effects of NO2. Studies generally reported a positive excess risk for asthmatics, and there was emerging evidence that CVD may cause persons to be more susceptible, though it is difficult to distinguish the effect of NO2 from other traffic pollutants. Children and older adults (65+ years) may be more susceptible than adults, possibly due to physiological changes occurring among these age groups.

In addition to intrinsically susceptible groups, a portion of the population may be at increased vulnerability due to higher exposures, generally people living and working near roadways. A considerable fraction of the population resides, works, or attends school near major roadways. Of this population, those with physiological susceptibility will have even greater risks of health effects related to NO2.