

# Aria più pulita, polmoni più sviluppati nei bambini

La più importante rivista di Medicina al mondo è il *The New England Journal of Medicine* NEJM. Anche quest'anno il NJEM ha voluto riproporre ai suoi lettori una raccolta selezionata (in formato abstract + editoriale allegato) dei 12 migliori lavori pubblicati dalla rivista nel 2015.

Tra questi si segnala il seguente "**Association of Improved Air Quality with Lung Development in Children**" - **Associazione tra il miglioramento della qualità dell'aria e sviluppo del polmone in bambini**", articolo di fondamentale importanza che va fatto girare in tutte le Reti che lottano per la Salute. Questo si conclude con un'affermazione inequivocabile e di capitale importanza per la salute dei nostri bambini:

**"Abbiamo scoperto che i miglioramenti a lungo termine della qualità dell'aria sono stati associati con effetti positivi statisticamente e clinicamente significativi sulla crescita della funzione polmonare nei bambini"**.

Di seguito, inoltre, l'Editoriale altrettanto importante dal titolo inequivocabile: "**Cleaner Air, Bigger Lungs**" - **Aria più pulita, polmoni più sviluppati**.

## Notable article of 2015 – NEJM

### Association of Improved Air Quality with Lung Development in Children

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## BACKGROUND

Air-pollution levels have been trending downward progressively over the past several decades in southern California, as a result of the implementation of air quality-control policies. We assessed whether long-term reductions in pollution were associated with improvements in respiratory health among children.

## METHODS

As part of the Children's Health Study, we measured lung function annually in 2120 children from three separate cohorts corresponding to three separate calendar periods: 1994–1998, 1997–2001, and 2007–2011. Mean ages of the children within each cohort were 11 years at the beginning of the period and 15 years at the end. Linear regression models were used to examine the relationship between declining pollution levels over time and lung-function development from 11 to 15 years of age, measured as the increases in forced expiratory volume in 1 second (FEV<sub>1</sub>) and forced vital capacity (FVC) during that period (referred to as 4-year growth in FEV<sub>1</sub> and FVC).

## RESULTS

Over the 13 years spanned by the three cohorts, improvements in 4-year growth of both FEV<sub>1</sub> and FVC were associated with declining levels of nitrogen dioxide (P<0.001 for FEV<sub>1</sub> and FVC) and of particulate matter with an aerodynamic diameter of less than 2.5 μm (P= 0.008 for FEV<sub>1</sub> and P<0.001 for FVC) and less than 10 μm (P<0.001 for FEV<sub>1</sub> and FVC). These associations persisted after adjustment for several potential confounders. Significant improvements in lung-function development were observed in both boys and girls and in children with asthma and children without asthma. The proportions of children with clinically low FEV<sub>1</sub> (defined as <80% of the predicted value) at 15 years of age declined significantly, from 7.9% to 6.3% to 3.6% across the three periods, as the air quality improved (P=0.001).

## CONCLUSIONS

We found that long-term improvements in air quality were associated with statistically and clinically significant positive effects on lung-f function growth in children. (Funded by the Health Effects Institute and others.)

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## Editorial

### Cleaner Air, Bigger Lungs

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In the latter half of the 20th century, Los Angeles had, by many measures, higher levels of photochemical air pollutants than any other major city in the United States (Fig. 1). To address this problem, the California Air Resources Board and its partners became leaders in quantifying the health effects of air pollutants and in aggressively implementing pollution-control strategies. Even with these actions, air-pollution levels remained high. In 1993, “Health Advisories” were issued on 92 days.<sup>1</sup> In that year, the prospective Children’s Health Study was launched to examine the effects of air pollution on lung growth in children. Fourth-grade children were recruited from 12 communities in southern California with varying exposures to the pollutants of concern (ozone, nitrogen dioxide, and particulate matter). Repeated lung-function measurements were taken for these children for 8 years, the period of life during which the greatest growth of lung function occurs.

In this first cohort, children living in more polluted communities had lower cumulative lung growth during the follow-up period.<sup>2</sup> These results were important clinically because even modest reductions in attained lung function at maturity are predictive of respiratory disease, coronary heart disease, and reduced life expectancy.<sup>3</sup> Of course, such an association does not prove causality. However, the case for a causal relationship can be strengthened by consistent evidence from repeated studies. To that end, Gauderman and his colleagues enrolled two additional cohorts of children from the Children’s Health Study and found consistent associations between community air pollution and lung-function growth in the children recruited in 1993,<sup>2</sup> 1997,<sup>4</sup> and 2003.<sup>5</sup> The consistency of findings in the three separate cohorts is compelling. Moreover, the investigators sought to minimize the potential for confounding by controlling for known individual and community predictors of lung-function growth. Nevertheless, unmeasured or imperfectly measured characteristics of these communities, such as differences in ethnic background or socioeconomic status, may have confounded these analyses and produced a false positive association. Although lung-function growth and potential confounders were measured for each child, air pollution exposures were based on community means. Such studies have been described as “semi-individual”<sup>6</sup> with respect to the exposure variables. Thus, these analyses could also have been influenced by differences in community characteristics not captured in the individual data. A community is more than the aggregate of individual characteristics.<sup>7</sup> In this issue of the Journal, Gauderman et al.<sup>8</sup> examine the association between improvements in air quality and changes in lung-function growth from 11 to 15 years of age across these three cohorts of children. They show that 4-year growth in forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) improved as levels of air pollution (nitrogen dioxide and particulate matter with an aerodynamic diameter of <2.5  $\mu\text{m}$  [PM2.5] and <10  $\mu\text{m}$  [PM10]) declined in five of these communities.

This study provides corroborating information because the analyses are based on comparisons within communities and thus are not confounded by differences between communities.

The potential confounders of these temporal comparisons are characteristics of the communities that changed during the period of study.

Recall that, to be a confounder, a variable must be associated with both air-pollution levels and lung-function growth. The advantage of these complementary approaches is that characteristics of the communities are less likely to confound both spatial and temporal comparisons.

In the original Children's Health Study cohort design, communities were selected to represent extremes of exposure to particulate matter, nitrogen dioxide, and ozone air pollution. For example, in 1994 mean concentrations of PM<sub>2.5</sub> ranged from 31.5 µg per cubic meter (in Mira Loma) to 6.7 µg per cubic meter (in Santa Maria), and the nitrogen dioxide level ranged from 36.4 ppb (in Long Beach) to 2.7 ppb (in Lompoc).<sup>9</sup> Between 1994 and 2010, the period analyzed by Gauderman et al., changes in PM<sub>2.5</sub> and nitrogen

dioxide levels within the five study communities approached the between-community differences in 1994. For example, the mean PM<sub>2.5</sub> level improved from 31.5 µg per cubic meter (1994–1997) to 17.8 µg per cubic meter (2007–2010) in Mira Loma, and the nitrogen dioxide level improved from 34.4 ppb (1994–1997) to 20.3 ppb (2007–2010) in Long Beach. Temporal changes in ozone, however, were modest.

These results suggest that the children born after air-pollution levels had declined in these communities had greater lung-function growth. These investigators had previously shown, in a relatively small number of children, that participants who moved out of the study area to cleaner communities had improved lung-function growth, whereas those who moved to more polluted communities had reduced growth.<sup>10</sup> This raises the possibility that some of the loss of lung function associated with exposure to air pollution is reversible.

In recent years, much of the research on the effects of community air pollution has focused on premature death and on clinical events such as myocardial infarctions or hospital admissions. Because these events occur primarily among older adults, there has been less interest in intermediate physiological (subclinical) measures.

Nevertheless, there is growing awareness of the effects of early life events on the risk of adult-onset chronic diseases. Reduced lung function is a powerful predictor not only of chronic respiratory disease in adults but also of chronic cardiovascular disease. The reported net deficits in lung function in children living in the more polluted communities may provide a partial explanation for the associations between air-pollution levels and mortality rates observed both in southern California<sup>11</sup> and nationally.<sup>12</sup>

Some have argued that the substantial improvements in air quality over the past 40 years are sufficient to protect public health and that there is little evidence to support more stringent standards. However, the current report and other studies suggest that further improvement in air quality may have beneficial public health effects.

Four decades ago, most Americans were exposed to much higher levels of air pollution than those observed today.

At that time, it was difficult to find communities with little or no exposure, which limited the ability of investigators to determine a "no-effect level." With the improvements in air quality, observational studies can now assess the benefits of reductions in air-pollution exposure into the range below those historical levels. These new observational studies often show that there are health benefits associated with improvements in air quality even when the pollution levels are within a range previously thought to be safe.



**Figure 1. Pollution in Los Angeles.**

Los Angeles is shown in the late 1980s (Panel A) and in 2014 (Panel B).

Ted Spiegel/Corbis (Panel A), Ted Soqui/Corbis (Panel B)

*Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.*

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1. The Southland's war on smog: fifty years of progress toward clean air (through May 1997). Diamond Bar, CA: South Coast Air Quality Management District (<http://www.aqmd.gov/home/library/public-information/publications/50-years-of-progress>).

2. Gauderman WJ, Avol E, Gilliland F, et al. The effect of air pollution on lung development from 10 to 18 years of age. *N Engl J Med* 2004;351:1057-67. [Erratum, *N Engl J Med* 2005;352:1276.]
3. Hole DJ, Watt GC, Davey-Smith G, Hart CL, Gillis CR, Hawthorne VM. Impaired lung function and mortality risk in men and women: findings from the Renfrew and Paisley prospective population study. *BMJ* 1996;313:711-5.
4. Gauderman WJ, Gilliland GF, Vora H, et al. Association between air pollution and lung function growth in southern California children: results from a second cohort. *Am J Respir Crit Care Med* 2002;166:76-84.
5. Urman R, McConnell R, Islam T, et al. Associations of children's lung function with ambient air pollution: joint effects of regional and near-roadway pollutants. *Thorax* 2014;69:540-7.
6. Künzli N, Tager IB. The semi-individual study in air pollution epidemiology: a valid design as compared to ecologic studies. *Environ Health Perspect* 1997;105:1078-83.
7. Diez-Roux AV. Bringing context back into epidemiology: variables and fallacies in multilevel analysis. *Am J Public Health* 1998;88:216-22.
8. Gauderman WJ, Urman R, Avol E, et al. Association of improved air quality with lung development in children. *N Engl J Med* 2015;372:905-13.
9. Peters JM, Avol E, Navidi W, et al. A study of twelve Southern California communities with differing levels and types of air pollution. I. Prevalence of respiratory morbidity. *Am J Respir Crit Care Med* 1999;159:760-7.
10. Avol EL, Gauderman WJ, Tan SM, London SJ, Peters JM. Respiratory effects of relocating to areas of differing air pollution levels. *Am J Respir Crit Care Med* 2001;164:2067-72.
11. Jerrett M, Burnett RT, Ma R, et al. Spatial analysis of air pollution and mortality in Los Angeles. *Epidemiology* 2005;16:727-36.
12. Pope CA III, Burnett RT, Thun MJ, et al. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 2002;287:1132-41.

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