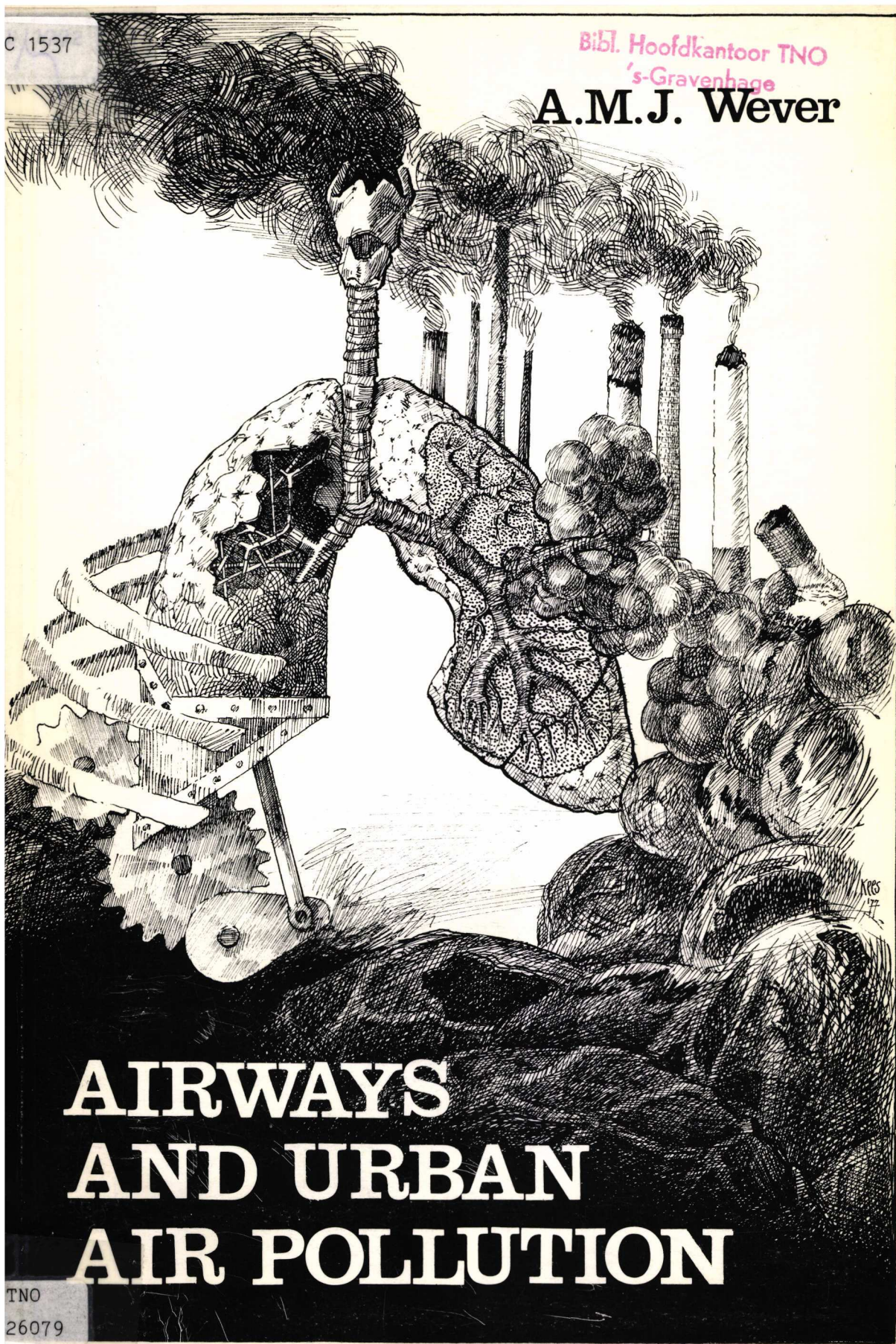


A.M.J. Wever



AIRWAYS AND URBAN AIR POLLUTION

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9 JULI 1982

1. Het verdient aanbeveling meer onderzoek te verrichten naar de effecten van stikstof monoxide op de luchtwegen.
2. Bij kortdurende pieken in de luchtverontreiniging dient men erop bedacht te zijn dat respiratoire symptomen pas na één of meerdere dagen kunnen optreden.
3. The chief problems of preventive medicine are two:
(i) to prove beyond doubt that such modalities as exercise, low-fat diets, and a 55-mile-an-hour speed limit are cost-effective, and (ii) to persuade a pleasure-loving, affluent, and undisciplined society to accept the necessary warnings. (Science 193: 837, 1976).
4. De termen prospectief en retrospectief duiden onvoldoende het karakter van een epidemiologisch onderzoek aan en kunnen derhalve beter vermeden worden.
5. Het verdient aanbeveling bij patiënten met diffuse longaandoeningen van onbekende aard een thoracospie met een longbiopsie à vue te verrichten.
6. De oorzaak van het ziektebeeld van de primaire pulmonale hypertensie dient niet in de longarteriolen gezocht te worden, maar in het longparenchym zelf.
7. In de gezondheidszorg verdienen nazorgprogramma's voor patiënten met chronische obstructieve longaandoeningen meer aandacht.
8. Het is momenteel onmogelijk de ontwikkeling van ernstige longfunctiestoornissen vroegtijdig te voorspellen.

9. Bij de preventie van kinderastma dienen atopische ouders geadviseerd te worden omtrent het meest gewenste tijdstip van de conceptie.
10. De in de kliniek gehanteerde normaalwaarden zijn slecht gefundeerd.
11. De feitelijke psychosociale begeleiding van de ziekenhuispatiënt en de opvattingen en verwachtingen die de patiënt hierover heeft, komen niet overeen. (T. Soc. Geneesk. 54: 810, 1976).
12. Een vaste verzorgster in de eerste 18 levensmaanden van een kind is van kardinaal belang voor zijn psychische en sociale ontplooiing.
13. In het "Repertorium Verpakte Geneesmiddelen" dienen zowel de prijzen van de genoemde geneesmiddelen vermeld als ook de generische namen in het register opgenomen te worden.
14. De veiligheid van de zebra-oversteekplaats kan vergroot worden door de "zebra" negentig graden te draaien en met reflecterende verf te beschilderen.

SULPHUR DIOXIDE

0.05	ppm	=	0.145	mg/m ³
0.1	ppm	=	0.290	mg/m ³
0.2	ppm	=	0.580	mg/m ³
0.3	ppm	=	0.870	mg/m ³
0.4	ppm	=	1.16	mg/m ³
0.5	ppm	=	1.45	mg/m ³
1	ppm	=	2.9	mg/m ³
2.5	ppm	=	7.2	mg/m ³
5	ppm	=	14.5	mg/m ³
10	ppm	=	29	mg/m ³
50	ppm	=	145	mg/m ³
100	ppm	=	290	mg/m ³

NITROGEN DIOXIDE

0.1	ppm	=	0.188	mg/m ³
0.5	ppm	=	0.94	mg/m ³
1	ppm	=	1.88	mg/m ³
2	ppm	=	3.76	mg/m ³
5	ppm	=	9.4	mg/m ³
10	ppm	=	18.8	mg/m ³
25	ppm	=	47	mg/m ³
50	ppm	=	94	mg/m ³
100	ppm	=	188	mg/m ³

OZONE

0.05	ppm	=	0.098	mg/m ³
0.10	ppm	=	0.196	mg/m ³
0.25	ppm	=	0.490	mg/m ³
0.37	ppm	=	0.725	mg/m ³
0.50	ppm	=	0.980	mg/m ³
0.75	ppm	=	1.47	mg/m ³
1	ppm	=	1.96	mg/m ³
2.5	ppm	=	4.9	mg/m ³
5	ppm	=	9.8	mg/m ³

SULPHUR DIOXIDE

0.100	mg/m ³	=	0.034	ppm
0.250	mg/m ³	=	0.085	ppm
0.500	mg/m ³	=	0.170	ppm
0.750	mg/m ³	=	0.255	ppm
1	mg/m ³	=	0.340	ppm
1.5	mg/m ³	=	0.510	ppm
5	mg/m ³	=	1.7	ppm
10	mg/m ³	=	3.4	ppm
50	mg/m ³	=	17	ppm
100	mg/m ³	=	34	ppm
200	mg/m ³	=	68	ppm
300	mg/m ³	=	102	ppm

NITROGEN DIOXIDE

0.100	mg/m ³	=	0.05	ppm
0.500	mg/m ³	=	0.27	ppm
1	mg/m ³	=	0.53	ppm
5	mg/m ³	=	2.66	ppm
10	mg/m ³	=	5.32	ppm
20	mg/m ³	=	10.6	ppm
50	mg/m ³	=	26.6	ppm
100	mg/m ³	=	53.2	ppm
200	mg/m ³	=	106.4	ppm

OZONE

0.100	mg/m ³	=	0.051	ppm
0.250	mg/m ³	=	0.128	ppm
0.500	mg/m ³	=	0.255	ppm
0.750	mg/m ³	=	0.382	ppm
1	mg/m ³	=	0.510	ppm
1.5	mg/m ³	=	0.765	ppm
2	mg/m ³	=	1.02	ppm
5	mg/m ³	=	2.55	ppm
10	mg/m ³	=	5.1	ppm

Stichting Hooftkantoor TNO
's-Gravenhage
9 JULI 1982

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An epidemiological study in
matched pairs in the Rijnmond area

COVER DESIGN: KEES PUTMAN
© A. M. J. WEVER

RIJKSUNIVERSITEIT TE GRONINGEN

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matched pairs in the Rijnmond area

PROEFSCHRIFT

TER VERKRIJGING VAN HET DOCTORAAT
IN DE GENEESKUNDE
AAN DE RIJKSUNIVERSITEIT TE GRONINGEN
OP GEZAG VAN DE RECTOR MAGNIFICUS
DR. M.J. JANSSEN IN HET OPENBAAR TE VERDEDIGEN OP
WOENSDAG 2 MAART 1977
DES NAMIDDAGS TE 4 UUR

DOOR

ANTONIUS MATTHEUS JOHANNES WEVER

geboren te Tilburg

PROMOTOR

PROF. DR. N.G.M. ORIE

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*To ALL who contributed
with word and deed
thought and feat*

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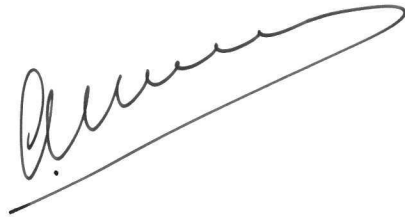
To those who were the subjects

To those who carried out the investigation

To those who were helpful in the processing and analyzing of the data

To those who made the presentation of this thesis possible

The cooperation, enthusiasm, and interest I met so often during the investigation was highly appreciated!

A handwritten signature in dark ink, featuring a series of connected loops and a long, sweeping underline that extends to the right.

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INTRODUCTION

In the autumn of 1971 a severe air pollution episode occurred in the Rijnmond area which is the most polluted area in the Netherlands because of an established large complex of petrochemical industries. This episode led to many complaints of malodour and irritation of the airways. Public opinion reacted intensely against the pollution of the environment and many official and unofficial voices were heard demanding that responsible industries should be forced to stop their production processes temporarily and that more forced control on industries should be exerted. However, before any far-reaching measures could be taken it was felt that research should be devoted to the special air pollution situation in the Rijnmond area. In order to assess and objectify the medical complaints raised the Local Authorities of Vlaardingen, which town experiences the heaviest air pollution in this area, invited the TNO Research Unit for Epidemiology of Chronic Non-Specific Lung Disease to organize an epidemiological study with financial aid from the Central Government, which invitation was kindly accepted. This present study, which took place in 1973, is a day by day follow-up study during one year by means of a diary technique in order to examine a possible association between air pollution levels and respiratory symptoms and lung function values. Changes in the severity of the manifestations of the chosen respiratory parameters can be considered mainly in relation to a hyperreactivity of the airways to exogenous non-specific stimuli (in this case air pollutants) which is one of the basic mechanisms of causing the obstructive syndrome of Chronic Non-Specific Lung Disease (CNSLD).

It was decided to take as population in Vlaardingen only women. Most of them being housewives the disturbing effects of expo-

sure to occupational air pollution are less than in men. Furthermore, women are more often non-smokers or less severe smokers than men. The disadvantage of a female population is, however, the lower prevalence rate of CNSLD in females as compared with males, and allergic factors being more pronounced than bronchial hyperreactivity in females with CNSLD.

To find out whether the respiratory reactions to air pollution differed according to degree of CNSLD the sample taken was divided into four subgroups from no CNSLD up to severe CNSLD.

To eliminate as far as possible the concomitant effects of meteorological conditions a female control population was chosen in a relatively low polluted district of Rotterdam only 15 kilometers away from Vlaardingen. Matched pairs were formed with regard to age, smoking habit, and degree of CNSLD.

The following possible disturbing factors could not be accounted for satisfactorily in this epidemiological study:

Exposure to indoor air pollution which varies according to type of housing and smoking habits of the residents (Biersteker et al., 1965);

Exposure to biological air pollution which is very difficult to measure qualitatively and quantitatively;

Intercurrent viral respiratory infections which are difficult to objectify in a large scale diary study;

A possible *self-selection* for medical reasons of the population living at present in the Rijnmond area.

With this epidemiological study, however, it is hoped to supply useful information on the medical aspects of the air pollution situation in the Rijnmond area and to contribute a piece of a stepping stone.

CHAPTER I

AIR POLLUTION

1. DEFINITION.

According to a WHO Expert Committee on Environmental Sanitation (WHO, 1958) air pollution can be defined as follows: "Air pollution is limited to the situations in which the outdoor ambient atmosphere contains material in concentrations which are harmful to man or to his environment". In this definition, however, only outdoor ambient atmosphere is considered as being of importance, but later it has been shown that the indoor ambient atmosphere is also of importance in air pollution problems (Biersteker et al., 1965; Lefcoe and Inculet, 1971, 1975).

A broad definition of air pollutants has been given by Chambers: "Those substances added in sufficient concentrations to the air to produce a measurable effect on man or other animals, on vegetation or on material. These substances may therefore include almost any natural or artificial composition of matter capable of being airborne" (Chambers, 1968). In this sense two discrete types of air pollution can be distinguished:

1. *Chemical air pollution* which is made up of inorganic and organic material, and occurs mainly as a result of industrialization and urbanization. Therefore the term "urban air pollution" will be used in this thesis. However, also natural phenomena such as volcanic eruptions, sandstorms, and forest fires can cause chemical air pollution.
2. *Biological air pollution* which is formed by organic material such as house dust mites, pollen, fungi, actinomycete spores, animal proteins, and viruses. As the biological air pollution is beyond the scope of this thesis it will not be dealt with any further.

2. CRITERIA FOR AIR QUALITY.

Attempts have been made to set out criteria for air quality in order to determine which levels of air pollution may be accepted or to what extent levels of air pollution should be reduced in order to prevent any adverse effect on health.

In 1963 a WHO Inter-regional Symposium on "Criteria for Air Quality and Methods of Measurement" set out such criteria for air quality to be presented as four "Levels" of concentrations, exposure times, and corresponding effects (WHO, 1964). These "Levels" are defined as follows:

- Level I: Concentrations and exposure times at or below which, according to the present knowledge, neither direct nor indirect effects (including alteration of reflexes or of adaptive or protective reactions) have been observed.
- Level II: Concentrations and exposure times at and above which there is likely to be irritation of the sensory organs, harmful effects on vegetation, visibility reduction, or other adverse effects on the environment.
- Level III: Concentrations and exposure times at and above which there is likely to be impairment of vital physiological functions or changes that may lead to chronic diseases or shortening of life.
- Level IV: Concentrations and exposure times at and above which there is likely to be acute illness or death in susceptible groups of the population.

In the United States of America the 1967 Amendments to the Clean Air Act required "the development of such criteria of air quality as may be requisite for the protection of the public health and welfare. Such criteria shall reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of an air pollution agent".

Under this Act "*Air Quality Criteria*" have been issued by the U.S. Department of Health, Education and Welfare for: particulate matter, sulphur oxides, nitrogen oxides, carbon monoxide, hydrocarbons, and photochemical oxidants.

For industrial purposes *Threshold Limit Values* (TLV) -or *Maximum Allowable Concentrations* (MAC)- have been established, which indicate an "approximate empirical level of concentration of a potentially hazardous airborne aerosol which will cause no lung disease -or very little- in workers exposed to it over a period of a working life" (Parkes, 1974). These threshold limit values refer to time-weighted concentrations during a 7 or 8 hour working day and a 40 hour working week. However, one must not extrapolate TLV's to ambient air. The TLV's should be divided by a safety factor, a "guesstimate", in order to arrive to ambient air quality standards or *Maximum Immissible Concentrations* (MIC). A few examples of TLV's and derived MIC values are given in table 1.1.

3. HISTORY.

Smoke was the first pollutant attention was drawn to in publications when in the 13th century coal was introduced for heating as a substitute for wood fuel. In its early introduction the use of coal was prohibited in London by an Act which was passed by Parliament in 1273. In the 16th century this law had apparently been relaxed and the use of coal became more widely used.

By 1600 sulphur was the second pollutant identified in the burning process of coal and it was thought to cause irritation of the throat and nose.

In the late 19th and early 20th century the rising chemical and metallurgic industries contributed to a large extent to the increase of sulphur dioxide and other pollutants (e.g. nitrogen dioxide, hydrogen sulphide, fluorides, and heavy metals) in the atmosphere.

In 1863 the first "Alkali Act" was established in Great

Table 1.1. Examples of TLV's and derived MIC's
for some air pollutants.

	TLV in mg/m^3	MIC ¹⁾ in $\mu\text{g/m}^3$
aldehydes:		
acetaldehyde	180	1800
acrolein	0.25	1.25
formaldehyde	3	15
carbon black	3.5	17.5
hydrocarbons:		
benzene	30	150
styrene	420	4200
xylene	0.1	0.5
nitrogen monoxide	30	300
nitrogen dioxide	9	45
ozone	0.2	1
sulphur dioxide	13	65

¹⁾ Maximum Immissable Concentrations given as maximum yearly averages.

(Source: Nota Milieunormen deel 1+2, Gedeputeerde Staten van de provincie Groningen).

Britain, and it required that "specific trade processes giving off noxious and offensive gases may not be used or operated unless the owner has obtained a certificate of Registration and renewed it annually. Even then the best practical means must be used so as to prevent pollution". This first Alkali Act covered about 80 works and this number was raised gradually to 2200 with about 3500 separate processes in 1962.

After the Second World War new sources of pollution appeared when motor traffic in conurbations increased gradually especially causing the release of nitrogen oxides and hydrocarbons, which gave rise to a particular type of smog called "photochemical smog", first described in Los Angeles in 1943. This photochemical smog occurs only under certain conditions (see section 5.2.7.).

Although much work and much concern was devoted to the air pollution problem it took several acute air pollution disasters (the Meuse Valley in 1930, Donora in 1948, London in 1952) to accelerate both the research on the effects of air pollution and the efforts in its control. One of the early results that emerged from all these efforts was the "Clean Air Act" passed in Great Britain in 1956.

The main objectives of the Clean Air Act were:

- The prohibition of "dark smoke" from any chimney subject to certain concessions.
- The control of new furnace installations by compulsory notification to the Local Authority with a system of "prior approval" where appropriate.
- The control of the heights of all new chimneys.
- The restriction of the emission of grit and dust.
- The empowering of Local Authorities to make smoke control areas.

Since the Clean Air Act became effective air pollution in the major cities of Great Britain has decreased considerably and no major smog episodes have occurred.

In the United States of America air pollution control was authorized mainly at State level, but in 1967 a federal "Clean Air Act" for all the States was enforced.

In the Netherlands two Acts deal with air pollution control, namely:

1. *Hinderwet* (Nuisance Act) of 1952. Under this Act conditions can be made to industries by the Local Authorities to prevent danger, damage or nuisance of the environment.
2. *Wet inzake de Luchtverontreiniging* (Air pollution Act) of 1970. Under this Act measures can be taken to restrain the pollution of the air. For example licences are required for industries which produce air pollution (to be granted by the Provincial Administration), and maximum immissable concentrations can be set by the Central Government.

In spite of all the efforts - both by Governments and Industries - in reducing the concentrations of pollutants in the atmosphere urban air pollution still remains a problem as industrialization expands and motor traffic continues to increase. Although the measures taken nowadays may be sufficient to prevent acute episodes of high pollution one should also take into consideration the possible effects of long-term exposure to ordinary levels of urban air pollution which may become manifest only after many years.

4. NATURE OF AIR POLLUTANTS.

4.1. ACCORDING TO THE ORIGIN.

The air pollutants can be divided according to their origin into two main groups:

1. "*Primary pollutants*":

Substances emitted from identifiable sources, such as: particles, and compounds of carbon, sulphur, nitrogen, and organic material.

2. "*Secondary pollutants*":

Substances produced in the air by interaction among two or more primary pollutants, or by reaction with normal atmospheric constituents, such as: acid mists, sulphuric acid in droplets, and substances formed by photochemical reactions.

4.2. ACCORDING TO THE PHYSICAL AND CHEMICAL CHARACTERISTICS.

A classification of air pollutants according to their physical and chemical characteristics is as follows (Katz, 1961):

1. *Particulates or particulate matter*:

They make up 10% of all air pollutants. The following distinctions can be made:

- a. *Solid particles*: usually irregular in shape; they exist either individually or as aggregations.
- b. *Liquid particles* (or droplets): usually spherical in shape.

Often the term *aerosol* is used which refers to a solid or liquid particle of about 0.01-10 μ in diameter, dispersed in a gaseous medium (e.g. sulphur trioxide aerosol, sulphuric acid aerosol). Particular types of aerosols are: smoke, fog, dust, haze, mist, and vapours.

The particulates can also be classified according to the measurement technique used:

- a. *Deposited particulate matter or dustfall*: particles greater than 10 μ in diameter and not respirable. This gives a valuable indication of the amount of fly ash and dust deposited.
- b. *Suspended particulate matter*: particles of 0.1-10 μ in diameter, usually suspended as an aerosol. The measurement of suspended particulate matter is a most valuable indicator of clinical relevant particulate matter.

2. *Gases*:

They make up 90% of all air pollutants. The most important gases are: sulphur dioxide, oxides of nitrogen, aldehydes, carbon monoxide, hydrocarbons, and photochemical oxidants.

5. SOURCES OF AIR POLLUTION.

5.1. MAIN SOURCES OF AIR POLLUTION.

The main sources of air pollution are the domestic heating (specially in former days), the industries, and the traffic. The "Beaver Committee" in their report (Committee on Air Pol-

lution, 1953) decided "to concentrate in the first place on air pollution arising from the combustion of fuels, as being the main cause of "smog" of the kind which did so much damage in London in December 1952 and which is recurring evil in many large towns". In this report they pointed out that domestic smoke, being discharged at low level and at low temperature, has the greatest effect on forming smog.

As the burning of coal for domestic heating has diminished considerably with the introduction of oil and natural gas, the main sources of air pollution now come from the industries and the traffic in densely populated western communities.

5.2. EMISSION SOURCES OF INDIVIDUAL AIR POLLUTANTS.

1. *Particulate matter:*

The particles greater than 10 μ originate from burning coal or incineration processes which are poorly controlled.

The particles less than 10 μ originate from burning oil, petrol, and diesel. Metallurgical processes in industries often cause these smaller particles. The particles may contain metallic elements (e.g. lead, iron, tin, asbestos) and non-metallic elements (e.g. carbon, sulphur).

2. *Sulphur dioxide:*

Sulphur dioxide (SO_2) originates from combustion processes of fuels containing sulphur, such as burning of coal and oil, and smelting of ores.

3. *Nitrogen oxides:*

Nitrogen monoxide or nitric oxide (NO) and nitrogen dioxide (NO_2) are the most important oxides of nitrogen as regards air pollutants. They emanate from all fuel combustion processes that take place at very high temperature (i.e. more than 2000°F , that is 1093°C). About one third of nitrogen oxides in the air is produced by motor vehicles. Most of the nitrogen oxides produced is in the form of NO which is subsequently oxidized in the atmosphere to NO_2 . When NO levels are low (about 1 ppm or 1.2 mg/m^3) this oxidation process is slow, but it is accelerated enormously by photochemical

processes. Although man-made nitrogen oxides are greatly exceeded by natural occurring nitrogen oxides formed by bacterial processes, the man-made emissions of nitrogen oxides are all concentrated in urban areas.

4. *Hydrocarbons*:

These pollutants are produced primarily by motor vehicles by incomplete combustion of petrol.

Many of the hydrocarbons may enter into photochemical reaction processes yielding oxidants and reducing agents. The hydrocarbons do not react primarily with sunlight but with oxygen atoms, excited oxygen, and with ozone.

Hydrocarbons are compounds whose molecules consist of atoms of hydrogen and carbon only, and the following groups can be distinguished:

a. *Aliphatic or acyclic* hydrocarbons: carbon atoms arranged in chains only, such as methane (CH_4). The paraffin, olephin, and acetylene hydrocarbons are classified in this group.

b. *Alicyclic* hydrocarbons: carbon atoms arranged in rings other than benzene rings, such as cyclohexane.

c. *Aromatic* hydrocarbons: carbon atoms arranged in benzene rings (six-membered carbon ring), such as benzene, styrene, and xylene.

5. *Aldehydes*:

In the photochemical oxidation of hydrocarbons and in the individual reactions of hydrocarbons with ozone and oxygen atoms aldehydes are formed which are in fact oxygenated hydrocarbon derivatives.

The main aldehydes are: formaldehyde (CH_2O), acrolein ($\text{CH}_2=\text{CHCHO}$), acetaldehyde (CH_3CHO).

In their turn the aldehydes also play a part in photochemical processes.

6. *Carbon monoxide*:

The principal source of carbon monoxide (CO) is the petrol engine which produces two third of all CO emissions. Other sources are all other incomplete combustions of carbonaceous

fuels, cigarette smoke (mainstream smoke contains up to 4% CO), and poorly flued domestic heating.

7. *Photochemical oxidants:*

A composition of secondary pollutants formed by photo-oxidation of hydrocarbons in the presence of nitrogen dioxide and aldehydes. This photo-oxidation process takes place under the influence of ultra-violet rays and gives rise to the formation of ozone and other oxidants such as peroxyacetyl-nitrate (PAN). The term "oxidants" is used because these products will oxidize certain reagents not readily oxidized by oxygen.

The formation of "photochemical smog" was first noticed in Los Angeles where the dense traffic, the situation of the city, and the meteorological conditions which often prevail in that area favour the formation of this particular type of smog.

Special conditions which are required in the photochemical smog formation are: high levels of nitrogen oxides and hydrocarbons, low wind speed, temperature inversion, and sufficient sunlight.

6. AIR POLLUTION AND THE ATMOSPHERE.

6.1. METEOROLOGICAL CONDITIONS AND AIR POLLUTION.

The levels of air pollution that will eventually be reached in ambient air depend not only on emissions from sources, but also for a great deal on the atmospheric conditions present. In fact, the atmosphere plays an important part in cleansing the air from the air pollutants (Neiburger, 1967). The two most important factors in this cleansing mechanism are:

1. *Wind velocity:* the wind is a transport factor of the air pollutants. The stronger its velocity, the more turbulent fluctuations will occur -both horizontally and vertically- which results in a dispersion of the pollutants.
2. *Vertical temperature gradient:* with increasing altitude the temperature declines and this gives rise to vertical con-

vection currents resulting in a vertical diffusion of the pollutants.

In a situation when cold air is near the ground and warm air is aloft, there will be no vertical air movements and the pollutants will not be diffused vertically. This situation is usually referred to as "inversion".

At high latitude inversions occur mainly when an anticyclone is present (winds being light or absent), particularly during colder parts of the year. In an anticyclone the air sinks and gets warmer by compression, and air near the ground cools by radiative heat loss especially at clear sky.

At low latitude inversions occur mainly in summer when a semi-permanent anticyclone is present over the oceans with air descending on its eastern side, so that the western continental coastal regions are mainly affected by inversions (e.g. Los Angeles, San Francisco).

After being diffused into the atmosphere the pollutants are removed from it by the following mechanisms (Wexler, 1961):

Gravitational settling (mainly large particles);

Impaction on surfaces on the earth (particles);

Precipitation after being accumulated in raindrops (particles, gases);

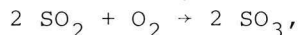
Absorption in the oceans, seas, and lakes (gases).

6.2. CHEMICAL AND PHYSICAL REACTIONS OF AIR POLLUTANTS IN THE ATMOSPHERE.

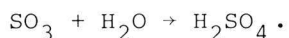
This problem has been studied for many years and still not everything yet is known about the innumerable processes which take place in the atmosphere, not only between air pollutants and the ambient air but also between the air pollutants themselves.

Some examples of known reactions in the atmosphere are:

a. SO_2 : During incineration processes this gas is partly oxidized to SO_3 :



when emitted this compound is converted to sulphuric acid:



The sulphuric acid in aerosol form gives rise to bluish

coloured smoke.

In the atmosphere the remainder of the SO_2 is slowly oxidized to sulphuric acid or sulphates.

b. NO : By various processes this gas is oxidized to NO_2 , sometimes slowly, sometimes more rapidly.

c. NO_2 : This brownish gas is gradually converted to nitric acid (HNO_3):



Nitric acid will eventually be removed from the atmosphere in rain droplets.

Also, NO_2 is dissociated into NO and atomic oxygen under the influence of ultra-violet rays.

d. Hydrocarbons: The main reaction of these pollutants is photo-oxidation yielding aldehydes and peroxy-compounds.

CHAPTER II

EFFECTS OF AIR POLLUTION ON THE AIRWAYS

1. INTRODUCTION.

To evaluate the effects of air pollution on the airways two main types of investigation can be distinguished: experimental (laboratory) studies on the pathological and physiological effects of air pollutants in animals and man, and epidemiological studies on the effects of air pollution in populations.

Experimental studies have been carried out to investigate the effects of individual air pollutants as well as combinations of air pollutants when inhaled by animals and man. Though animal studies may provide us with basic information on effects of air pollutants on airways, one should be very cautious in applying the results to human beings because of the anatomical and physiological differences between animals and man. Furthermore, in these animals such concentrations of pollutants were frequently used in combination with such exposure times as are likely never to be experienced by human beings in the ambient urban atmosphere.

Therefore, to get better and more useful information on possible effects of air pollutants on the human airways, exposures in man are much more important. However, ethical considerations have put a limitation to the actual studies carried out and most of the human data available are a result of experiments in volunteers.

The review of the animal studies will be restricted to more general conclusions because of the different exposure times, the different concentrations of pollutants, and also the dif-

ferent species of animals used such as mice, rats, guinea pigs, rabbits, dogs.

The experimental studies will be reviewed according to the type of air pollutant.

Epidemiological studies on the effects of air pollution have been carried out in populations in several parts of the world and have provided most useful information on the possible effects of air pollution on the airways, and the possible relationship between air pollution and respiratory disease. However, when comparing different epidemiological studies, it must be borne in mind that there are international differences in populations, in pollution composition, in length of exposure, and in level of exposure, while the composition of urban air pollution is so complex that it is almost impossible to denominate a specific air pollutant as being the cause of the effects found.

The epidemiological studies will be reviewed according to the type of air pollution exposure, i.e.: short-term exposure to high levels of urban air pollution, and long-term exposure to a general level of urban air pollution.

The review of the literature on experimental and epidemiological studies on effects of air pollution on the airways will be restricted to studies which can serve as background information to the present study. For further details and other studies the reader is referred to the General Literature on Air Pollution.

All concentrations will be expressed in $\mu\text{g}/\text{m}^3$ or mg/m^3 (1 mg = 1000 μg).

Conversion tables from mg/m^3 to ppm and from ppm to mg/m^3 are given in Appendix A for sulphur dioxide, nitrogen dioxide, and ozone.

2. DEFENSE MECHANISMS OF THE AIRWAYS TO INHALED AIR POLLUTANTS.

This subject has been reviewed by Green (1970) who considered the defense mechanisms of the airways as forming a protective

umbrella against a hostile environment while every man may be characterized by his own individual umbrella.

The defense mechanisms to inhaled gases and particles will be discussed successively.

2.1. INHALED GASES.

The defense possibilities of the airways to inhaled gases are small and consist of either absorption of the gas on the moist surface of the upper respiratory tract, or a detoxification process. The latter can take place either by chemical combination with pre-existing lung substance, or by an antagonist or inhibitor.

2.2. INHALED PARTICLES.

The defense possibilities of the airways to inhaled particles are more extensive and adequate than those to gases and they consist of either an aerodynamic filtration or a physical removal of the particles.

2.2.1. AERODYNAMIC FILTRATION OF PARTICLES.

Many particles even as small as $1\ \mu$ are deposited in the nose during normal breathing (Proctor et al., 1969) which demonstrates that nose-breathing is a very efficient mechanism for filtering particles.

In general the deposition of particles in the airways depends on the sedimentation, impaction, and diffusion of the individual particles which are functions of their aerodynamic diameters¹⁾ (Muir, 1972), while the amount of particles inhaled is proportional to the minute ventilation (Muir and Davies, 1967). Particles greater than $10\ \mu$ are mainly deposited in the nasopharynx, particles of $2\text{--}10\ \mu$ are mainly deposited in the tra-

¹⁾ The aerodynamic diameter (or size) of a particle expressed in microns (μ) is equivalent to the diameter of a sphere of Unit Density ($1\ \text{g/ml}$) which falls in air with the same terminal settling velocity as the particle.

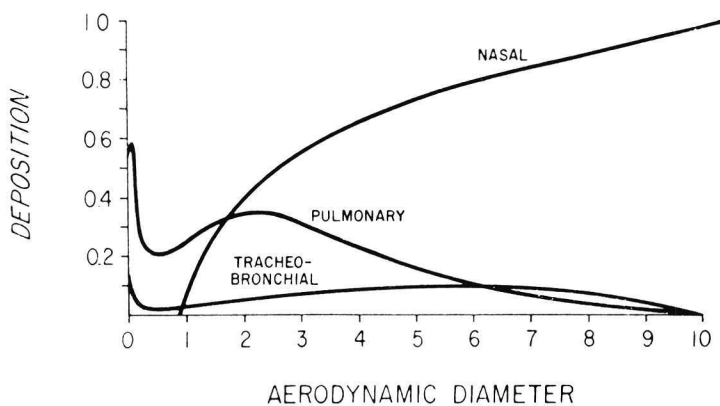


Fig. 2.1. Deposition as a function of particle size for 15 respirations/min, 750 cm³ tidal volume. (Reproduced from Health Physics, vol. 12, page 179, 1966, by permission of the Health Physics Society)

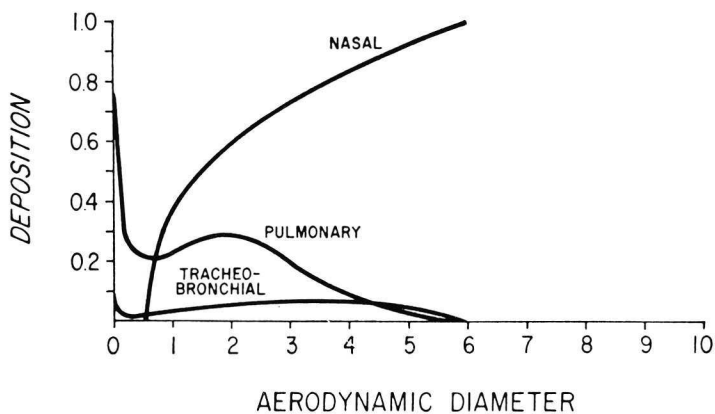


Fig. 2.2. Deposition as a function of particle size for 15 respirations/min, 2150 cm³ tidal volume. (Reproduced from Health Physics, vol. 12, page 179, 1966, by permission of the Health Physics Society)

cheobronchial tree, and particles of $0.5\text{--}2\text{ }\mu$ and less than $0.25\text{ }\mu$ are mainly deposited in the terminal airways. Particles of $0.25\text{--}0.5\text{ }\mu$ are mainly exhaled and their probability of being deposited is about 25%.

Two examples of theoretical calculations of the regional deposition of inhaled particles made by the Task Group on Lung Dynamics (1966) are shown in the figures 2.1. and 2.2.

2.2.2. PHYSICAL REMOVAL OF PARTICLES.

The physical removal is by mechanical clearance and by detoxification processes.

The *mechanical clearance* of particles from the airways is believed to consist of two phases: a rapid phase, representing the removal of particles from the ciliated regions by means of the mucociliary transport mechanism, and a slow phase, representing the removal of particles from non-ciliated regions, i.e. the terminal bronchioles and alveoli (Albert et al., 1967; Morrow et al., 1967).

In the *rapid phase* a half life¹⁾ of particles from about 19 minutes up to 4 hours in normal subjects has been observed (Albert and Arnett, 1955; Toigo et al., 1963; Albert et al., 1967; Morrow et al., 1967; Luchsinger et al., 1968; Thomson and Short, 1969; Pavia et al., 1970; Thomson and Pavia, 1973). The differences in the half life of particles found is likely to be due to the differences in nature and size of the particles used. The mucociliary transport mechanism is thought to be affected in patients with obstructive pulmonary disease and Toigo et al. (1963) found slower clearance rates in patients with chronic lung disease (half life more than 4 hours). However, Luchsinger et al. (1968) and Thomson and Short (1969) could not confirm this and later Thomson and Pavia (1974) found even faster clearance rates in patients with chronic bronchitis compared with a group of normal subjects which may be due to impairment of deep penetration of particles into the lungs of bronchitics.

¹⁾ Half life: 50% of the particles cleared.

Another factor that may act upon the mucociliary transport mechanism is the smoking of cigarettes. The effect of smoking a few cigarettes seems to be a stimulation of the clearance rate (Albert et al., 1975). Also, a slowing of the mucociliary clearance rate was observed in smokers when they abstain from smoking (Camner and Philipson, 1972; Albert et al., 1973) and re-suming smoking after abstaining caused an increase in clearance rate (Albert et al., 1975). As a chronic effect of smoking cigarettes a general decrease in the clearance rate has been reported by Albert et al. (1969), Lourenço et al. (1971), and Bohning et al. (1975), while Luchsinger et al. (1968) and Thomson and Pavia (1973) found no differences in the clearance rate between smokers and non-smokers.

The mechanical clearance of particles from the non-ciliated regions - the *slow phase* - is believed to take place after phagocytosis by alveolar macrophages at three different levels:

- an alveolar fluid flow (half life of particles about 24 hours);
- an interstitial fluid flow (half life of particles about 100 hours);
- a perivascular clearance of particles by cell breakdown (half life of particles about 60 to 100 days).

The in situ *detoxification* of particles may take place by the following mechanisms: phagocytosis, non-phagocytic processes¹⁾, immunological processes, and the formation of granulomata (Green, 1970).

3. EXPERIMENTAL STUDIES IN ANIMALS AND MAN ON THE EFFECTS OF AIR POLLUTANTS ON THE AIRWAYS.

3.1. INTRODUCTION.

Studies on the following air pollutants will be reviewed: particulate matter, sulphur dioxide, nitrogen oxides, hydrocarbons, aldehydes, ozone, carbon monoxide, and photochemical oxidants.

¹⁾ Wetting of particles, action of surface enzymes and interferon.

As a reference to the possible concentrations of some air pollutants in the ambient atmosphere the reader is referred to table 6.4., p. 101.

3.2. PARTICULATE MATTER: carbon particles and smoke.

3.2.1. INTRODUCTION.

In general particulate matter may be effective in the following ways (Air Quality Criteria for Particulate Matter, 1969):

- the particle may interfere with the clearance of other inhaled toxic materials;
- the particle may act as a carrier of an adsorbed toxic substance, and hence produce a potentiating effect or occasionally reduce the toxicity of a second pollutant;
- the particle may give rise to a pathological or physiological response;
- the particle may be intrinsically toxic, due to its inherent chemical and/or physical characteristics, for example beryllium and asbestos leading to Berylliosis respectively Asbestosis, and sulphuric acid aerosols.

Studies on the effects of the intrinsically toxic particles will be excluded from the review.

3.2.2. STUDIES IN ANIMALS.

Pathological effects.

In exposures for short periods (up to about 3 days) pulmonary oedema and blocking of the airways were observed when animals were exposed to high concentrations of smoke (over 700 mg/m^3) (Pattle et al., 1959). Lower concentrations of smoke showed no toxic effects and after three months only phagocytosis and clearance from the lung were seen (Pattle and Burgess, 1957; Salem and Cullumbine, 1961).

In exposures for prolonged periods Schnurer and Haythorn (1937) found fibrous reactions around carbon particles (smoke concentrations of $4410 \text{ particles/m}^3$). However, Nau et al. (1962) could not demonstrate any toxic effects using concentrations of $1.6\text{--}2.4 \text{ mg/m}^3$, and Vintinner and Baetjer (1951) observed

no increase in susceptibility to infections.

Physiological effects.

An increase in flow resistance¹⁾ was observed in several experiments in which aerosols were used (Amdur, 1958; Amdur and Corn, 1963; Amdur and Underhill, 1968). The effects were dependent on the particle size, the aerosol concentration, and on the number of particles (Amdur and Corn, 1963).

The increase in resistance after inhalation of particulate matter is thought to be a vagal reflex bronchoconstriction via lung irritant receptors with vagal afferent fibres (Widdicombe et al., 1962).

3.2.3. STUDIES IN MAN.

Dubois and Dautrebande (1958) found an increase in airway resistance²⁾ in healthy persons after inhalation of dust particles, with no effect on the total lung capacity and the vital capacity; however, in patients with pulmonary disease a decrease in vital capacity was observed. An increase in airway resistance was also observed by Mc Dermott (1962) when coal dust clouds were inhaled in concentrations of 19 mg/m³ or more for 4 hours, lower concentrations showed no effects on the airway resistance.

This increase in airway resistance in man reflects a bronchoconstriction presumably due to a reflex (Widdicombe et al., 1962; Simonsson et al., 1967).

3.2.4. SUMMARY.

Both in animal and human experiments an increase in lung resistance³⁾ was found which is thought to be due to a reflex bronchoconstriction via parasympathetic pathways. The effects

1) Flow resistance: total lung resistance, measured by means of the pressure flow method.

2) Airway resistance: total lung resistance minus tissue resistance, measured by means of a body-plethysmograph.

3) (Total) lung resistance: airway resistance plus tissue resistance.

were dependent on the concentration, the size, and the number of particles. As the response in man showed a great variation there may exist an individual sensitivity to inhaled particulate matter.

3.3. SULPHUR DIOXIDE (SO_2).

3.3.1. STUDIES IN ANIMALS.

Pathological effects.

When animals were exposed to such concentrations of SO_2 (ranging from about 1700-14.000 mg/m^3) that death occurred the main pathological changes seen were occlusion of bronchioles and venous congestion in animals with a short survival, and pulmonary oedema in animals with a long survival (Leong et al., 1961).

Changes in the mucosa of the trachea and bronchi with increasing number of mucus secreting cells and thickening of the mucus blanket were observed by Dalhamn and Rhodin (1956) and by Reid (1963) in long-term exposures to SO_2 (concentrations ranging from about 30-1160 mg/m^3). From later experiments Dalhamn (1961) reported reversible cessation of ciliary beat.

Physiological effects.

Several observers reported an increase in flow resistance of the lungs, using concentrations of SO_2 ranging from 460 $\mu\text{g}/\text{m}^3$ to 2400 mg/m^3 (Amdur, 1957; Salem and Aviado, 1961; Amdur, 1966). An increase in nasal resistance was observed by Frank and Speizer (1965), using concentrations of 20-660 mg/m^3 .

The increase in resistance after exposure to SO_2 is thought to be caused by a reflex bronchoconstriction via parasympathetic pathways in both upper and lower respiratory tract.

Strandberg (1964) found that the absorption of SO_2 by the nasal mucosa was less efficient at low than at high concentrations of SO_2 , and Amdur (1966) obtained a straight line dose-response relationship when the absorption data obtained by Strandberg were applied, relating the increase in pulmonary flow resistance to the concentration of SO_2 . The data obtained by Strand-

Table 2.1. Summary of experimental studies in animals exposed to sulphur dioxide.

SPECIES	CONCENTRATION		LENGTH OF	EFFECT	REFERENCE
	mg/m ³	ppm	EXPOSURE		
PATHOLOGICAL EFFECTS					
rats	29	10	6 hours/day for 10 weeks	reduced mucus flow; amount of secretion greatly increased; morphological changes in epithelium of trachea	Dalhamn and Rhodin, 1956
rabbits	870	300		cessation of ciliary beat within 45 min.	Dalhamn, 1961
mice, rats, guinea pigs	1700-14000	600-5000	until death occurred (up to 4 hours)	occlusion of bronchioles and venous congestion; pulmonary oedema	Leong et al., 1961
rats	870-1160	300-400	more than 3 months	increase in number of mucus-secreting cells; thickening of mucus blanket; excessive mucus in bronchial lumen	Reid, 1963
PHYSIOLOGICAL EFFECTS					
guinea pigs	up to 720	up to 250	1 hour	increase in pulmonary flow resistance	Amdur, 1957
dogs	580-2450	200-850	1-4 minutes	bronchoconstriction	Salem and Aviado, 1961
dogs	20-665	7-230	15 minutes	increase in nasal resistance	Frank and Speizer, 1965
guinea pigs	0.460-2420	0.16-835	1 hour	increase in resistance; dose-response curve	Amdur, 1966

berg (1964) and Frank et al. (1967) show that at high concentrations SO_2 is absorbed for 90% or more by the nasal mucosa. A summary of the experimental studies is given in table 2.1.

3.3.2. STUDIES IN MAN.

After inhalation of SO_2 an increase in respiratory frequency was found by Amdur et al. (1953) using concentrations of 3-23 mg/m^3 , which could not be confirmed by Lawther (1955). An increase in lung resistance -either measured as pulmonary flow resistance or as airway resistance- was observed at concentrations ranging from about 3-87 mg/m^3 of SO_2 in exposures of short duration (Frank et al., 1962; Speizer and Frank, 1966). These experiments showed an individual sensitivity to SO_2 , and the increase in resistance seems to be related to the concentration of SO_2 used and not so much to the duration of exposure. When SO_2 was administered by the nose the increase in lung resistance was less than when administered by the mouth (Speizer and Frank, 1966) which observation was thought to be due to a greater absorption of the SO_2 by the nasal mucosa (Frank and Speizer, 1964; Speizer and Frank, 1966). This latter phenomenon was also observed in animal studies.

Lawther and Waller (1973) showed that in quiet breathing SO_2 is largely absorbed in the upper respiratory tract and that deep breathing is necessary to elicit effects (i.e. an increase in airway resistance). Their experiments in man showed that there is a wide range of individual sensitivity to SO_2 .

Andersen et al. (1974) found a decrease in $\text{FEV}_{1.0}$ at concentrations of SO_2 as low as 2.9 mg/m^3 and suggested an existence of a nasobronchial reflex.

Gökemeijer et al. (1973) found marked bronchoconstriction in patients with CNSLD after inhalation of 29 mg/m^3 of SO_2 for three minutes which effect could largely be blocked by a beta-2 receptor stimulating drug. Later Gökemeijer (1976) reported a dose-response relation using concentrations of 14.5, 29, and 43.5 mg/m^3 of SO_2 in patients with CNSLD, while at these concentrations subjects without any signs of CNSLD showed no bron-

Table 2.2. Summary of experimental studies in man exposed to sulphur dioxide.

CONCENTRATION mg/m ³	CONCENTRATION ppm	LENGTH OF EXPOSURE	EFFECT	REFERENCE
2.9-23	1-8	10 minutes	shallower and more rapid respiration	Amdur, 1953
2.9, 14.5, and 37	1, 5, and 13	10-30 minutes	increase in airway resistance at 2.9 mg/m ³ in 1 subject, at 14.5 mg/m ³ in 9 subjects, at 37 mg/m ³ in all 11 subjects	Frank et al., 1962
43.5 and 81	15 and 28	10 minutes	increase in pulmonary flow resistance	Speizer and Frank, 1966
29	10	3 minutes	increase in viscous work of breathing in patients with CNSLD	Gökemeijer et al., 1973
2.9	1	25 deep breaths	3 out of 12 subjects showed significant increase in airway resistance	Lawther and Waller, 1973
14.5, 29, 43.5, 58, and 87	5, 10, 15, 20, and 30	10 minutes	sulphur dioxide largely absorbed in the upper respiratory tract	Lawther and Waller, 1973
2.9, 14.5, and 72.5	1, 5, and 25	6 hours	decrease in FEV _{1.0} and increase in nasal air- flow resistance	Andersen et al., 1974
14.5, 29, and 43.5	5, 10, and 15	3 minutes	decrease in FEV _{1.0} in patients with CNSLD	Gökemeijer, 1976

choconstriction.

However, no effects were reported by Burton et al. (1969) after inhalation of about $3-9 \text{ mg/m}^3$ of SO_2 for thirty minutes, and by Gökemeijer (1976) after inhalation of SO_2 of less than 7 mg/m^3 for three minutes.

A summary of the experimental studies is given in table 2.2.

3.3.3. SUMMARY.

In animal studies pathological changes were observed, the duration of exposure and the concentration of SO_2 - which was in general very high - playing an important part.

As a physiological effect an increase in lung resistance in animals and in man was observed, which is believed to be caused by a bronchoconstriction due to a reflex (Nadel et al., 1965; Simonsson et al., 1967). Gökemeijer et al. (1973) observed in patients with CNSLD effects indicating an interaction of SO_2 with either alpha- or beta-receptor enzyme systems. The physiological effects seem to be related to the concentration of SO_2 used, and besides there are strong indications of an individual sensitivity to SO_2 .

3.4. COMBINATIONS OF SULPHUR DIOXIDE AND PARTICULATE MATTER.

3.4.1. STUDIES IN ANIMALS.

Pathological effects.

An increased mortality in mice and guinea pigs was found by Pattle and Burgess (1957) when SO_2 was administered in combination with particulate matter. Salem and Cullumbine (1961) found a variable effect of smoke on the toxicity of SO_2 depending on the animal species used. Gross et al. (1967) found cellular thickening of the alveolar wall, which was not observed when smoke alone was administered.

No increased susceptibility to pulmonary infections could be demonstrated when using a combination of particulate matter and SO_2 (Vintinner and Baetjer, 1951).

Physiological effects.

In the experiments in guinea pigs by Amdur (1957; 1963; 1968)

it was demonstrated that some aerosols could potentiate the effect of SO_2 as measured by pulmonary flow resistance. The particle size (the smaller particles possibly have a greater synergistic effect than the bigger particles because of a deeper penetration into the lungs), the particle concentration, the sulphur dioxide concentration, and the humidity of the respiratory tract (McJilton et al., 1973) were found to be important factors.

The aerosols that seem to have a potentiating effect on sulphur dioxide are those aerosols of soluble salts which dissolve SO_2 and also possibly catalyze the oxidation of sulphur dioxide to sulphuric acid which is more irritant to the respiratory tract than SO_2 (Amdur, 1958; Amdur, 1968). However, Corn et al. (1972) could not confirm Amdur's findings in cats using sodium chloride aerosols.

3.4.2. STUDIES IN MAN.

Snell and Luchsinger (1969) reported a slight potentiating effect of a distilled water aerosol on the response to sulphur dioxide while a saline aerosol exerted no effect. Other investigators also found no potentiating effects of saline aerosols on the response to sulphur dioxide (Frank et al., 1964; Burton et al., 1969).

3.4.3. SUMMARY.

In some animal species a potentiating effect of certain aerosols on the response to sulphur dioxide could be demonstrated, but studies on man failed to demonstrate a conclusive effect possibly due to the lower concentrations of sulphur dioxide used in these experiments.

3.5. NITROGEN OXIDES (NO_x).

3.5.1. INTRODUCTION.

The nitrogen oxides to be discussed are nitrogen monoxide (NO) and nitrogen dioxide (NO_2). When NO is present in high concentrations in the atmosphere it is rapidly converted to NO_2 , so it is difficult to control concentrations of NO in experimental

studies. Therefore, many more studies are carried out on the effects of NO_2 . A review of the effects of the nitrogen oxides will be given with regard to the respiratory system only.

3.5.2. NITROGEN MONOXIDE (NO).

In animals no adverse effects on the respiratory function were observed at concentrations up to 94 mg/m^3 of NO (Murphy et al., 1964).

As far as known no studies of experimental exposure to nitrogen monoxide on man have been reported.

3.5.3. NITROGEN DIOXIDE (NO_2).

3.5.3.1. STUDIES IN ANIMALS.

Pathological effects.

Concentrations greater than 190 mg/m^3 of NO_2 are lethal to most animal species. In most cases pulmonary oedema was found (La Towsky et al., 1941).

Acute - reversible - pathological changes of the pulmonary tissue have been observed after short-term exposures to nitrogen dioxide using concentrations ranging from $940 \text{ } \mu\text{g/m}^3$ - 190 mg/m^3 . The severity of the changes tends to increase with increasing concentration of NO_2 and seems to depend less on the duration of exposure. The following changes were observed:

- mast cell degeneration (Thomas et al., 1967);
- hyperplasia of bronchial epithelium (Kleinerman and Cowdrey, 1968);
- removal of cilia from the terminal bronchiolar epithelium (Bils, 1974);
- acute inflammatory reaction of bronchial epithelium (Kleinerman and Wright, 1961);
- basal membrane damage and intra-alveolar oedema (Dowell et al., 1971).

Chronic pathological changes of the pulmonary tissue have been observed after long-term exposures to nitrogen dioxide, either continuously or intermittently, using concentrations ranging from $940 \text{ } \mu\text{g/m}^3$ - 47 mg/m^3 . The severity of the changes seems to be a function of the product of concentration and exposure time

Table 2.3. Summary of experimental studies in animals exposed to nitrogen dioxide with respect to pathological effects.

SPECIES	CONCENTRATION		LENGTH OF EXPOSURE	EFFECT	REFERENCE
	mg/m ³	ppm			
rats, guinea pigs, rabbits	141-188	75-100	2 hours	acute inflammatory reaction	Kleinerman and Wright, 1961
mice	6.6	3.5	2 hours	increased susceptibility to experimentally induced bacterial infections	Purvis and Ehrlich, 1963
rats	47	25	40 days	emphysema like lesions	Freeman and Haydon, 1964
mice	9.4	5	2 hours	increased susceptibility to experimentally induced bacterial infections	Ehrlich, 1966
rats	0.940	0.5	4 hours	mast cell degeneration	Thomas et al., 1967
rats	1.9	1	1 hour	mast cell degeneration	Thomas et al., 1967
mice	0.940	0.5	6-24 hours per day up to 12 months	increased susceptibility to experimentally induced bacterial infections	Ehrlich and Henry, 1968
rats	3.8	2	continuously	lesions of the terminal bronchiolar epithelium	Freeman et al., 1968 ^a
rats	18.8-47	10-25	continuously	emphysema like lesions	Freeman et al., 1968 ^b

Table 2.3. (continued)

hamsters	84.6-103		10 weeks	hyperplasia bronchial epithelium	Kleinerman and Lowdry, 1968
mice	0.940	0.5	6-24 hours, and 3-12 months	"pneumonitis" and early focal emphysematous lesions	Blair et al., 1969
squirrel monkeys	18.8 9.4	10 5	1 month 2 months	increased susceptibility to experimentally induced bacterial infections	Henry et al., 1970
beagle dogs	5.6-30	3-16	1 hour	intra-alveolar oedema at concentrations of 7 ppm or higher; membrane damage without oedema at lower concentrations	Dowell et al., 1971
squirrel monkeys	1.9	1	continuously for 16 months	slight emphysema and thickened bronchial and bronchiolar epithelium only in animals exposed to NO ₂ and challenged with influenza virus	Fenters et al., 1973
mice	14 4.3	7 2.3	4 hours 17 hours	increased susceptibility to experimentally induced bacterial infections	Goldstein, 1973
squirrel monkeys	56	30	3 hours	removal of cilia from terminal bronchiolar epithelium	Bils, 1974

Table 2.4. Summary of experimental studies in animals exposed to nitrogen dioxide with respect to physiological effects.

SPECIES	CONCENTRATION		LENGTH OF EXPOSURE	EFFECT	REFERENCE
	mg/m ³	ppm			
guinea pigs	10-24.5	5.2-13	2-4 hours	increase in respiratory rate and a decrease in tidal volume	Murphy et al., 1964
rats	1.5	0.8	continuously	increase in respiratory rate	Freeman et al., 1966
rabbits	15-22.5	8-12	continuously	increase in pulmonary flow resistance	Davidson et al., 1967
squirrel monkeys	65.8 and 94	35 and 50	2 hours	increase in respiratory rate and a decrease in tidal volume	Henry et al., 1969
squirrel monkeys	9.4	5	2 months	increase in respiratory rate and a decrease in tidal volume	Henry et al., 1970
	18.8	10	1 month		
beagle dogs	1.21 NO ₂ ⁺ 0.31 NO ₂ ⁻	0.63 NO ₂ ⁺ 0.25 NO ₂ ⁻	16 hours per day for 61 months	reduced peak expiratory flow and reduced diffusion capacity	Lewis et al., 1974

(Freeman et al., 1969). The following changes were observed:

- lesions of the terminal bronchiolar epithelium (Freeman et al., 1968^a);
- pneumonitis and early focal emphysematous lesions (Blair et al., 1969);
- emphysema like lesions (Freeman and Haydon, 1964; Freeman et al., 1968^b; Fenters et al., 1973).

Increased susceptibility to experimentally induced bacterial infections was observed in both short-term exposures to NO₂ (Purvis and Ehrlich, 1963; Ehrlich, 1966; Goldstein et al., 1973) and long-term exposures to NO₂ (Ehrlich and Henry, 1968; Henry et al., 1970). The impairment of the pulmonary antibacterial defense mechanism by nitrogen dioxide is thought to be due to alveolar macrophage dysfunction (Gardner et al., 1969), and occurs when a certain threshold limit of NO₂ is reached (Goldstein et al., 1973).

Physiological effects.

An increase in the respiratory frequency and a decrease in the tidal volume was observed after short-term exposures to about 10-95 mg/m³ of NO₂ (Murphy et al., 1964; Henry et al., 1969) and long-term exposures to about 1.5-17 mg/m³ of NO₂ (Freeman et al., 1966; Henry et al., 1970). Exposures to NO₂ in concentrations of 15-22.5 mg/m³ resulted in an increase in pulmonary flow resistance (Davidson et al., 1967). A reduced peak expiratory flow rate and a reduced diffusion capacity was observed after exposure to 1.21 mg/m³ of NO₂ (in combination with 0.31 mg/m³ of NO), while exposure to 0.27 mg/m³ of NO₂ (in combination with 2.05 mg/m³ of NO) yielded no effect on the respiratory function (Lewis et al., 1974).

A summary of the experimental studies is given in the tables 2.3. and 2.4.

3.5.3.2. STUDIES IN MAN.

Accidental exposures to very high concentrations of NO₂ have been reported in silo-fillers and in welders causing pneumonia and pulmonary oedema with subsequent bronchiolitis fibrosa

obliterans (Grayson, 1956; Lowry and Schuman, 1956; Norwood et al., 1966).

In volunteers an increase in airway resistance was observed after inhalation of 9.4 mg/m^3 of NO_2 for 10 minutes (Abe, 1967).

3.5.4. SUMMARY.

It has been shown that NO_2 is probably the most important compound of the nitrogen oxides.

Acute pathological changes of the bronchial epithelium and of the alveolar membrane, and chronic pathological changes at the level of the terminal bronchiolus with emphysematous lesions were found in animals as a result of exposure to NO_2 , depending on concentration and exposure time. Besides, an increased susceptibility to experimentally induced bacterial infections was observed. Both in animals and in man effects of exposure to NO_2 -in excessively high concentrations- on the pulmonary function were observed.

3.6. HYDROCARBONS.

The most important property of the hydrocarbons is the possibility to enter into photochemical processes forming products such as aldehydes (see section 3.7.) and ozone (see section 3.8.) which are more toxic to the respiratory tract than the hydrocarbons themselves. As for the toxicity of the hydrocarbons the reader is referred to the Air Quality Criteria for Hydrocarbons (1970) in which the animal and human experimental studies on hydrocarbons are extensively reviewed.

As a summary of these studies one can state that:

- the aromatic hydrocarbons are the most important group of hydrocarbons as regards adverse health effects;
- the hydrocarbons exert a toxic effect in man at concentrations from about 80 mg/m^3 ;
- the main toxic effects of the hydrocarbons are irritation of the mucous membranes of the eyes and the nose, and irritation of the upper respiratory tract; at high concentrations the central nervous system in animals was also found to be affected;

- exposure to hydrocarbons in animals can give rise to an increase in pulmonary flow resistance and in tidal volume, and to a decrease in respiratory frequency.

3.7. ALDEHYDES.

As the experimental studies in animals and man are also extensively reviewed in the Air Quality Criteria for Hydrocarbons (1970) only the main points will be presented here, the more so because the first importance of the aldehydes lies in their participation in photochemical processes:

- the main aldehydes with regard to adverse health effects are formaldehyde, acetaldehyde, and acrolein;
- the main toxic effects of the aldehydes are irritation of the mucous membranes of the eyes and the nose, and irritation of the upper respiratory tract;
- an increase in pulmonary flow resistance and in tidal volume, and a decrease in respiratory frequency can be found in animals as a result of exposure to acrolein at concentrations from $1615 \mu\text{g}/\text{m}^3$ (0.6 ppm);
- in man a toxic effect can be expected with exposures to formaldehyde at concentrations from about $2460 \mu\text{g}/\text{m}^3$ (2 ppm), to acrolein at concentrations from about $675 \mu\text{g}/\text{m}^3$ (0.25 ppm), and to acetaldehyde at concentrations from about $90 \text{ mg}/\text{m}^3$ (50 ppm);
- exposure to formaldehyde at high concentrations can cause pulmonary haemorrhage and oedema in animals, and serious inflammation of the upper and lower respiratory tract and bronchopneumonia in man.

3.8. OZONE.

3.8.1. STUDIES IN ANIMALS.

Pathological effects.

Short-term exposures to ozone at concentrations from $1960 \mu\text{g}/\text{m}^3$ gave rise to desquamative and degenerative epithelial changes in bronchi and bronchioli and acute pulmonary oedema (Scheel et al., 1959), and to degeneration of alveolar epithelial lining

Table 2.5. Summary of experimental studies in animals exposed to ozone with respect to pathological effects.

SPECIES	CONCENTRATION		LENGTH OF EXPOSURE	EFFECT	REFERENCE
	mg/m ³	ppm			
mice, hamsters	2.55 1.65	1.30 0.84	3 hours 4 hours 5 days per week for 2 weeks	increased susceptibility to experi- mentally induced bacterial infection	Miller and Ehrlich, 1958
mice	1.96	1	4 hours	superficial desquamation of epithelium and mild degree of acute oedema	Scheel et al., 1959
mice	6.27	3.2	4 hours	acute pulmonary oedema, and degenera- tive and desquamative changes of epithelium	Scheel et al., 1959
rabbits	16.25 up to 89.35	8.3 up to 45.6	1 hour every week for 49 weeks	fibrotic proliferation in the walls of the bronchiolar and alveolar ducts	Scheel et al., 1959
guinea pigs	1.96-9.8	1-5	2 hours	increased mortality as a result of an increased susceptibility to intra- venously administered histamine	Easton and Murphy, 1967
rabbits	0.59	0.3	3 hours	impairment of phagocytic properties of alveolar macrophages	Coffin et al., 1968
mice	8.8	4.5	2 hours every third day for 75 days	acute inflammatory and epithelial changes	Werthamer et al., 1970

Table 2.5. (continued)

mice	1.29-8.33	0.66-4.25	4 hours	decrease in pulmonary bactericidal activity	Goldstein et al., 1971
rabbits	9.8	5	3 hours	morphological alterations in the pulmonary alveolar macrophages	Huber et al., 1971
dogs	1.96-5.88	1-3	8-24 hours daily for 18 months	changes of the terminal and respiratory bronchiolar walls and epithelium	Freeman et al., 1973
squirrel monkeys	5.88	3	3 hours	degeneration of alveolar epithelial lining	Bils, 1974
rats	1.07-1.76	0.55-0.90	continuous, up to 6 months	fibroblastic activity at the junction of respiratory bronchioli and alveolar ducts	Freeman et al., 1974
mice	4.9	2.5	2 hours daily for 120 days	epithelial changes of trachea, bronchi, and bronchioli (metaplasia and hyperplasia)	Penha and Werthamer, 1974
rats	0.980-176	0.5-0.9	up to 48 hours	epithelial changes of terminal bronchioli and proximal alveoli	Stephens et al., 1974

Table 2.6. Summary of experimental studies in animals exposed to ozone with respect to physiological effects.

SPECIES	CONCENTRATION		LENGTH OF EXPOSURE	EFFECT	REFERENCE
	mg/m ³	ppm			
rats	3.9	2	3 hours	decrease in tidal volume; increase in respiratory frequency	Scheel et al., 1959
guinea pigs	0.67	0.34	2 hours	decrease in tidal volume; increase in respiratory frequency	Murphy et al., 1964
guinea pigs	2.12	1.08	2 hours	increase in flow resistance	Murphy et al., 1964
guinea pigs	9.8-13.7	5-7	2 hours	increase in flow resistance; decrease in lung compliance	Easton and Murphy, 1967
rats	1.96	1	6 hours	increased mortality due to exercise	Stokinger, 1965

(Bils, 1974). At lower concentrations epithelial changes in the terminal bronchioles and proximal alveoli were found (Stephens et al., 1974).

After intermittent long-term exposures to ozone at concentrations from $4900 \mu\text{g}/\text{m}^3$ morphological changes of the tracheal, bronchial, and bronchiolar epithelium were found (Scheel et al., 1959; Werthamer et al., 1970; Penha and Werthamer, 1974).

Long-term exposures to ozone at concentrations from $1960 \mu\text{g}/\text{m}^3$ resulted in morphological changes of the terminal and respiratory bronchiolar walls and epithelium (Freeman et al., 1973). A characteristic fibroblastic activity at the level of the junction of the respiratory bronchiole and the alveolar duct was noted by Freeman et al. (1974).

An increased susceptibility to experimentally induced bacterial infections was observed in both short-term and long-term exposures to ozone which gave rise to an increased mortality (Miller and Ehrlich, 1958). This increased susceptibility to infections is thought to be caused by an impairment of the phagocytic activity of alveolar macrophages resulting in an inhibition of the bactericidal activity of the lungs (Coffin et al., 1968; Goldstein et al., 1971; Huber et al., 1971; Goldstein et al., 1974), and probably occurs when a certain threshold limit of ozone is reached (Goldstein et al., 1974).

Easton and Murphy (1967) found an increased mortality as a result of an increased susceptibility to histamine after short-term exposure to ozone.

Physiological effects.

The following physiological effects were observed after short-term exposures to ozone at concentrations ranging from 670-13700 $\mu\text{g}/\text{m}^3$:

- a decrease in tidal volume and an increase in respiratory frequency (Scheel et al., 1959; Murphy et al., 1964);
- an increase in flow resistance (Murphy et al., 1964; Easton and Murphy, 1967);
- a decrease in lung compliance (Easton and Murphy, 1967);
- an increased mortality due to the performance of exercise during the exposure to ozone (Stokinger, 1965).

A summary of the experimental studies is given in the tables 2.5. and 2.6.

3.8.2. STUDIES IN MAN.

The effect of exposure to ozone on the respiratory tract manifests itself in respiratory symptoms and changes in respiratory function.

Several investigators reported one or more of the following symptoms as a result of exposure to ozone at concentrations from $500 \mu\text{g}/\text{m}^3$: substernal discomfort, cough, wheezing, dyspnoea, and irritation of the upper respiratory tract (Young et al., 1964; Bates et al., 1972; Hackney et al., 1975). The severity of the symptoms tended to increase with increasing concentration of ozone.

The following changes in respiratory function were observed after exposure to ozone at concentrations from $725 \mu\text{g}/\text{m}^3$:

- a reduction in forced vital capacity and timed forced expiratory volume (Young et al., 1964; Hazucha et al., 1973; Hackney et al., 1975; Kerr et al., 1975);
- a reduction in maximum flow at 50% of the vital capacity (Bates et al., 1972; Hazucha et al., 1973; Hackney et al., 1975);
- a reduction in maximum mid-expiratory flow rate (Hazucha et al., 1973);
- an increase in airway resistance (Goldsmith and Nadel, 1969; Bates et al., 1972; Kagawa and Toyama, 1975; Kerr et al., 1975);
- an increase in residual volume and in closing capacity¹⁾ (Hazucha et al., 1973).

Kerr et al. (1975) reported that a group of non-smokers had a greater response to exposure to ozone with regard to respiratory symptoms and respiratory function than a group of smokers.

¹⁾ Closing capacity: sum of closing volume and residual volume, expressed as percentage of total lung capacity

Closing volume: volume of the lungs at which the airways at the bottom of the lung start to close, expressed as percentage of the vital capacity.

Table 2.7. Summary of experimental studies in man exposed to ozone.

CONCENTRATION mg/m ³	ppm	LENGTH OF EXPOSURE	EFFECT	REFERENCE
1.18-1.57	0.6-0.8	2 hours	reduction in forced vital capacity, forced expiratory volume, and diffusion capacity for carbon monoxide	Young et al., 1964
1.96	1	1 hour	increase in airway resistance in all 4 subjects	Goldsmith and Nadel, 1969
1.47	0.75	2 hours	reduction of $\dot{V}_{max}$ at 50% VC; increase in airway resistance	Bates et al., 1972
0.725 and 1.47	0.37 and 0.75	2 hours	reduction of $\dot{V}_{max}$ at 50% VC, FVC, FEV _{1.0} , and MMFR; increase in residual volume and in closing capacity	Hazucha et al., 1973
0.725	0.37	2 hours	reduction in FVC and FEV _{1.0}	Hackney et al., 1975 ^a
0.980	0.50	4 hours	reduction in FVC and FEV _{1.0} and in $\dot{V}_{max}$ at 50% VC	Hackney et al., 1975 ^b
1.76	0.9	5 minutes	marked decrease in airway conductance when subjects undertook exercise	Kagawa and Toyama, 1975
0.980	0.5	6 hours	increase in airway resistance; decrease in FVC and FEV _{3.0}	Kerr et al., 1975

A great individual variation in the response to exposure to ozone was seen in most studies pointing to an individual threshold limit (Goldsmith and Nadel, 1969; Bates et al., 1972; Hackney et al., 1975). Subjects with a history of respiratory symptoms tended to respond to exposure to ozone at lower concentrations than subjects without such a history (Hackney et al., 1975). However, Gökemeijer (1976) found no effect on the viscus work of breathing in patients with CNSLD after exposure to up to 29.4 mg/m^3 of ozone for 3 minutes.

There is an indication that successive exposures to ozone have a cumulative effect (Hackney et al., 1975).

A summary of the experimental studies is given in table 2.7.

3.8.3. SUMMARY.

In animals exposure to ozone resulted in morphological changes of the epithelium of the respiratory tract up to the level of the proximal alveoli, and in physiological changes.

An increased susceptibility to bacterial infections was found, probably due to the observed impairment of the phagocytic activity of the alveolar macrophages as a result of exposure to ozone.

In man exposure to ozone can give rise to a variety of respiratory symptoms and to a decrement in respiratory function. There is an indication of an individual threshold limit. Moreover, persons with a history of respiratory symptoms and non-smokers seem to be more sensitive to exposure to ozone.

3.9. CARBON MONOXIDE.

In the experimental studies in animals and man carbon monoxide has been found to be inert to the respiratory tract at relatively low concentrations; its main toxicity lies in the reaction with heamoglobin to form carboxy-haemoglobin (Air Quality Criteria for Carbon monoxide, 1970). As the affinity of haemoglobin for carbon monoxide is about 200 times greater than for oxygen carboxy-haemoglobin is easily formed when carbon mon-

oxide is present in the inhaled air, affecting particularly the central nervous system and the cardiovascular system.

In man exposure to high concentrations of carbon monoxide - which may occur accidentally (e.g. in gas poisoning) or occupationally (e.g. in fire fighters) - can cause pulmonary oedema (Kittredge, 1971; Ogawa et al., 1974), but it is not clear whether this is due to a direct effect of carbon monoxide on the pulmonary tissue.

3.10. PHOTOCHEMICAL SMOG (PHOTOCHEMICAL OXIDANTS).

3.10.1. INTRODUCTION.

Photochemical smog is a naturally occurring complex mixture of air pollutants in which oxidants (ozone, nitrogen dioxide, and organic peroxides) are present as main compounds together with hydrocarbons and carbon monoxide in high concentrations. See for details on photochemical smog Chapter I, section 5.2.(7). For experimental purposes photochemical smog can be obtained either naturally from photochemical ambient air, or artificially by irradiation of exhaust or by mixing fixed concentrations of some of these pollutants.

3.10.2. STUDIES IN ANIMALS.

The following observations in animals were made after exposure to photochemical smog (at concentrations of "total oxidants" from 240-1960 $\mu\text{g}/\text{m}^3$):

- pathological changes of the alveolar cells and in the alveolar walls in mice (Bils, 1966; Bils and Romanovsky, 1967);
- an increase in pulmonary flow resistance (Murphy et al., 1963; Swann and Balchum, 1966; Wayne and Chambers, 1968; Lewis et al., 1974);
- an increased susceptibility to pulmonary infection in the latter half of the animal's lifetime (Hueter et al., 1966), and an increased mortality from bacterial pulmonary infection (Coffin and Blommer, 1967).

3.10.3. STUDIES IN MAN.

After exposures to a mixture of ozone, nitrogen dioxide, and carbon monoxide (at respective concentrations of up to 980 $\mu\text{g}/\text{m}^3$, 565 $\mu\text{g}/\text{m}^3$, and 35 mg/m^3) minor physiological changes were observed. These changes, however, did not occur consistently throughout all exposures (Hackney et al., 1975^a, 1975^b).

3.10.4. SUMMARY.

Exposures to photochemical smog resulted in only minor pathological and physiological changes in animals, while in man no consistent changes of the pulmonary function were observed.

In the experimental studies on photochemical smog concentrations were used as measured in the ambient atmosphere. Therefore, the effects were presumably less than after exposures to the individual photochemical pollutants used in artificially high concentrations.

3.11. SUMMARY OF THE EXPERIMENTAL STUDIES.

The *experimental studies on animals* have demonstrated that most of the reviewed urban air pollutants can exert adverse effects on the airways which manifest in pathological changes of the upper and lower respiratory tract, in physiological changes, and in disturbances of the pulmonary defense mechanism. The effects found were dependent on the concentration of the pollutants, the duration of the exposure, and on the animal species used in the experiments.

The animal studies can serve as a guide for experimental and epidemiological studies on man, and they suggest a real possibility that exposure to urban concentrations of air pollutants may damage the human airways.

The *experimental studies on man* have demonstrated that exposure to most of the reviewed urban air pollutants can result in respiratory symptoms and in a decrement in pulmonary function. Although most of the exposures were carried out at concentrations much higher than occur in acute episodes of air pollution, some investigators reported also effects on the airways using

concentrations of pollutants which are occasionally encountered in an urban environment.

The great variation in response which was often found forms a strong indication that there exists an individual sensitivity to particulate matter, sulphur dioxide, and ozone. Furthermore, there is some evidence that persons with (a history of) chronic obstructive pulmonary disease have a greater sensitivity to air pollutants than persons without such a history.

Except one study on ozone, no differences between smokers and non-smokers in response to exposures to air pollutants have been described.

Noteworthy is that the smoke from cigarettes contains a high concentration of nitrogen oxides (Haagen-Smit et al., 1959; Bokhoven and Niessen, 1961), of which nitrogen monoxide is the principal component at concentrations ranging from about 24-54 $\mu\text{g}/\text{m}^3$ per puff (450-1000 ppm) (Norman and Keith, 1965). About 10% of the nitrogen monoxide is probably converted in the airways to nitrogen dioxide (Freeman, 1975), which pollutant has been shown to be very toxic in experimental animal studies causing amongst other things emphysematous lesions. Indeed, in man some investigators have found evidence of an association between a history of smoking and the presence of emphysema in necropsy material (Ryder et al., 1971; Auerbach et al., 1972).

4. EPIDEMIOLOGICAL STUDIES ON THE EFFECTS OF AIR POLLUTION ON THE AIRWAYS.

4.1. INTRODUCTION.

In the epidemiological approach to the effects of urban air pollution on the airways mortality and morbidity data are used. *Mortality data* are obtained from death certificates which are tabulated in the vital records¹⁾ collected in most industrialized countries in the world.

¹⁾ Vital records: records of vital events, i.e. birth, death, marriage, and divorce.

Morbidity data can be obtained from several sources, the most important of which are in this context:

- general practitioner's records;
- hospital records;
- health and disease records of special populations, such as occupational groups, the armed forces, insured groups, old people's homes;
- morbidity studies: prevalence studies¹⁾ and longitudinal studies²⁾.

In a *prevalence study* the objective is to define the level of disease in a population at one point in time, i.e. the prevalence of disease.

In a *longitudinal study* the objective is to determine the frequency of disease over a period of time. The incidence of a disease can be measured which is the number of new cases of the disease in a specified period of time.

(MacMahon and Pugh, 1970).

When making national or international comparisons one should bear in mind the possibility of inaccuracy and incompleteness of the data, differences in definition and classification of diseases, and lack of standardization of the methods. This applies to mortality data as well as to morbidity data (Heasman, 1962; Reid, 1962; Mork, 1964; Reid and Rose, 1964; Alderson and Meade, 1967; MacMahon and Pugh, 1970; Reid, 1975).

The review of epidemiological studies on the effects of air pollution on the airways will be classified as follows:

1. Studies on the effects of short-term exposure to high levels of air pollution, to be subdivided in:
 - a. studies of acute episodes of high pollution: *acute effects*;
 - b. studies of intermittent subacute episodes of high pollution: *subacute effects*.

1) Prevalence study = point prevalence study = cross-sectional study.

2) Longitudinal study = cohort study = follow-up study.

2. Studies on the effects of long-term exposure to air pollution: *chronic effects*.

The levels of the major air pollutants found in a given epidemiological study will be expressed in micrograms per cubic meter ($\mu\text{g}/\text{m}^3$) as 24-hour averages, unless otherwise stated. As a reference to the possible concentrations of some air pollutants in the ambient atmosphere the reader is referred to table 6.4., p. 101.

4.2. STUDIES ON THE EFFECTS OF SHORT-TERM EXPOSURE TO HIGH LEVELS OF URBAN AIR POLLUTION.

4.2.1. ACUTE EPISODES OF HIGH POLLUTION: ACUTE EFFECTS.

4.2.1.1. EUROPE.

THE MEUSE VALLEY, December 1930.

During a severe fog in this valley which lasted five days 63 people died from a relatively small community and many more were affected with respiratory symptoms. Estimated maximum concentration of sulphur compounds was about $25,000 \mu\text{g}/\text{m}^3$ (Firket, 1931).

LONDON, November 1948.

During an episode of severe fog the maximum smoke level was $2780 \mu\text{g}/\text{m}^3$ and the maximum SO_2 level $2150 \mu\text{g}/\text{m}^3$.

Mortality: A substantial increase in mortality from all causes was observed during this period (Logan, 1949).

LONDON, December 1952.

During this episode smoke levels reached $4460 \mu\text{g}/\text{m}^3$ and sulphur dioxide levels $3830 \mu\text{g}/\text{m}^3$ (48-hour average).

Mortality: An excess number of deaths (4000) was observed in this period, especially in people over the age of 45 and in infants (Ministry of Health, 1954).

Morbidity: An excess number of claims for sickness benefits and an excess of hospital admissions especially for respiratory disease was observed (Ministry of Health, 1954). In a general practice the number of new cases of upper respiratory infections doubled and the number of lower respiratory infections trebled, which occurred mainly in people with known chronic respiratory

disease (Fry, 1953).

LONDON, January 1956.

Mortality: An increase in mortality (about 1000 excess deaths) from all causes in a fog episode, when the maximum level of smoke was $3250 \mu\text{g}/\text{m}^3$ and of SO_2 $1500 \mu\text{g}/\text{m}^3$, was reported (Logan, 1956).

LONDON, December 1957.

Morbidity: During a fog episode, when the maximum concentration of smoke was $2300 \mu\text{g}/\text{m}^3$ and of SO_2 $1600 \mu\text{g}/\text{m}^3$, an excess of applications to the Emergency Bed Service was observed (Bradley et al., 1958).

LONDON, December 1962.

The maximum concentration of smoke was $2000 \mu\text{g}/\text{m}^3$ and of SO_2 $3300 \mu\text{g}/\text{m}^3$.

Mortality: Martin (1966) reported an excess mortality of about 700 people particularly due to "bronchitis" and cardiovascular disease.

Morbidity: A 50% increase in new claims for sickness benefits was observed (Scott, 1963). A sudden appearance of "acute wheezy chests" was reported in a general practice (Fry et al., 1962).

ROTTERDAM (The Netherlands), January 1959, December 1962.

Mortality: An excess total mortality was found in the Rotterdam area during these fog episodes, when the maximum of the smoke levels reached $500 \mu\text{g}/\text{m}^3$ and of the SO_2 levels $1150 \mu\text{g}/\text{m}^3$ (Biersteker, 1966).

Morbidity: During the heavy fog in December 1962 an excess of applications to the Rotterdam City Emergency Bed Service was noted (Tesch, 1964; Biersteker, 1966), and a significant increase in the number of absentees from work because of respiratory illness was observed in Rotterdam's municipal employees (Biersteker, 1966).

VLAARDINGEN (the Netherlands), Autumn 1969.

The daily SO_2 values reached up to $400 \mu\text{g}/\text{m}^3$.

Morbidity: In a follow-up study, Van der Lende et al. (1975^a) found that in the majority of the persons lung function values were lower in the autumn of 1969 than in the autumn of 1972,

possibly as a result of a severe air pollution episode that happened to occur when the survey in 1969 took place.

4.2.1.2. UNITED STATES OF AMERICA.

DONORA, October 1948.

Mortality: A slight excess of deaths was found in the older age groups. Most of the deaths occurred on the third day of a 5-day episode of high pollution (Schrenk et al., 1949).

NEW YORK CITY, November 1953.

The maximum SO₂ level was 2460 µg/m³.

Mortality: A small increase in mortality distributed over all age groups was found (Greenburg et al., 1962).

Morbidity: An increase in attendances for respiratory disease to the out-patient department was observed in three out of four hospitals (Greenburg et al., 1962).

NEW YORK CITY, November, December 1962.

The maximum SO₂ level was 2145 µg/m³.

Mortality: An association between mortality in the ages of over 45 and SO₂ levels was found (MaCarroll and Bradley, 1966).

Morbidity: A significant increase in the number of respiratory infections was observed in people living in old people's homes (Greenburg et al., 1965).

NEW YORK CITY, November 1966.

The maximum SO₂ level was 1460 µg/m³.

Mortality: An excess number of deaths was noted (Glasser et al., 1967).

Morbidity: An increase in emergency visits for "bronchitis" and "asthma" was observed in three out of seven hospitals (Glasser et al., 1967). Data obtained with a questionnaire applied within 24 hours of the air pollution episode in white-collar workers in the New York Metropolitan Area showed an effect on the prevalence of respiratory symptoms, especially in workers with present or past history of respiratory disease (Becker et al., 1968).

NEW YORK CITY, Summer 1970.

Morbidity: During episodes of high pollution in the summer of 1970 data from telephone interviews showed significant in-

creases in "irritative" symptoms (eye irritation, throat irritation, chest discomfort, shortness of breath), when the levels of SO_2 respectively suspended particulate matter exceeded $320 \mu\text{g}/\text{m}^3$ and $145 \mu\text{g}/\text{m}^3$ (Cohen et al., 1974).

4.2.2. INTERMITTENT SUBACUTE EPISODES OF HIGH POLLUTION: SUBACUTE EFFECTS.

4.2.2.1. EUROPE.

LONDON.

Mortality: An increase in daily mortality was found during periods of heavy fogs between 1954 and 1957 when smoke levels were above about $2000 \mu\text{g}/\text{m}^3$ and SO_2 levels above about $1140 \mu\text{g}/\text{m}^3$ (Gore and Shaddick, 1958).

During the winter of 1958-1959 marked changes in mortality occurred above about $750 \mu\text{g}/\text{m}^3$ of smoke with about $710 \mu\text{g}/\text{m}^3$ of SO_2 . An increase in the death rate occurred with each abrupt rise in pollution within 24 hours (Martin and Bradley, 1960). This positive correlation, though weaker, was still found during the less polluted winter of 1959-1960 (Martin, 1964).

Morbidity: During several winters between 1954 and 1960 a consistent relationship was found between the degree of illness in bronchitic patients, as assessed by a diary technique, and the concentrations of smoke and SO_2 . The lowest concentration of smoke or SO_2 associated with any definite change in the patient's condition was about $600 \mu\text{g}/\text{m}^3$. No relationship was found with temperature or humidity (Waller and Lawther, 1955; 1957; Lawther et al., 1970). Lawther et al. (1970) found in the winter of 1964-1965 and again in the winter of 1967-1968 a lower correlation coefficient between the respiratory condition of their bronchitic patients and the concentrations of smoke and SO_2 as compared with their previous diary studies, admittedly because of reduced levels of air pollution during these winters. In their studies the minimum air pollution level leading to any significant response was found to be about $500 \mu\text{g}/\text{m}^3$ of SO_2 in combination with about $250 \mu\text{g}/\text{m}^3$ of smoke.

ROTTERDAM (the Netherlands).

Mortality: During the winter months of 1962 and 1963 a very weak correlation was found between SO₂ levels and daily mortality figures (Biersteker, 1966).

Morbidity: During the winter months of 1962 and 1963 no correlation could be demonstrated between air pollution and hospital admissions for respiratory disease (Biersteker, 1966).

4.2.2.2. UNITED STATES OF AMERICA.

NEW YORK CITY, 1960-1965.

Mortality: Glasser and Greenburg (1971) found an association between the mean number of daily deaths and the daily levels of SO₂ during the years 1960-1964 independent of weather conditions, although McCarroll and Bradley (1966) could only demonstrate such an association for some periods of high pollution during the years 1962-1964.

Morbidity: In a follow-up study in City residents between 1962 and 1965 an immediate effect of SO₂ with regard to eye symptoms and a delayed effect of SO₂ and particulate matter with regard to the symptom cough was found by McCarroll et al. (1967).

NEW YORK CITY, 1962-1965; PHILADELPHIA, 1963-1964; LOS ANGELES, 1962-1965.

Mortality: In a comparative study Lebowitz (1973) could demonstrate a relationship between daily mortality, and air pollution — weather.

LOS ANGELES.

Mortality: No relationship could be found between mortality from respiratory disease and episodes of high air pollution levels (Hechter and Goldsmith, 1961; Breslow, 1964).

Morbidity: Heimann (1964) reported as main complaints during smog episodes: eye irritation, excessive tear formation, and cough, occurring about midday. A significant increase in the mean number of attacks of asthma could be demonstrated in asthmatic patients when oxidant levels exceeded 250 µg/m³ (Schoettlin and Landau, 1961). A strong general effect of pollution on hospitalization (length of stay, frequency of admission) was observed for respiratory infections and allergic disorders

(Sterling et al., 1969). In a diary study in student nurses from 1961-1964 the average daily symptom rates for cough, chest discomfort, and eye irritation all increased with increasing maximum hourly oxidant pollution levels: from about 200 $\mu\text{g}/\text{m}^3$ for eye irritation, from about 390 $\mu\text{g}/\text{m}^3$ for chest discomfort, and from about 600 $\mu\text{g}/\text{m}^3$ for cough (Hammer et al., 1974). In a study in schoolchildren in 1966-1967 no significant changes in peak expiratory flow rate which correlated with changes in pollution level were found (McMillan et al., 1969). In a study in cross-country track runners an association was found between oxidant levels and athletic performance (Wayne et al., 1967). CALIFORNIA, 1970-1971.

Morbidity: In student populations of seven universities an association was found between the incidence of upper respiratory symptoms and air pollutants in particular oxidants, sulphur dioxide, and nitrogen dioxide. There was an indication that men and smokers of both sexes were more susceptible than others (Durham, 1974).

4.2.2.3. JAPAN:

TOKYO-YOKOHAMA AREA.

Mortality: Lebowitz et al. (1973) found a relationship between daily mortality and air pollution-weather in Tokyo in an analysis over a 3-yr. period.

Morbidity: The so called "Tokyo-Yokohama Asthma", described in American Military Personnel and occurring especially in the heavily polluted autumn and winter months (Huber et al., 1954), could not be demonstrated as being caused by episodes of high pollution only, but past history of bronchitis and smoking in combination with air pollution seems to be of importance (Phelps and Koike, 1962; Phelps, 1965). Moreover, no evidence of typical Tokyo-Yokohama Asthma was found in Japanese people (Oshima et al., 1964).

In Japanese schoolchildren Toyama (1964) found that peak flow rates varied according to the level of monthly air pollution measurements in a polluted area.

4.2.3. SUMMARY.

Short-term exposure to high levels of urban air pollution can give rise to an increase in mortality, particularly from respiratory disease, an increase in respiratory symptoms, and a decrement in pulmonary function. A certain level of air pollution must probably be reached before any effect - immediate or delayed - can be measured in a population.

Persons with a history of chronic pulmonary disease and persons in the older age groups seem to be most susceptible. As most morbidity studies were concerned with special groups one should be careful to generalize the results.

4.3. STUDIES ON THE EFFECTS OF LONG-TERM EXPOSURE TO URBAN AIR POLLUTION: CHRONIC EFFECTS.

4.3.1. NATIONAL COMPARATIVE STUDIES.

4.3.1.1. EUROPE.

GREAT BRITAIN.

Mortality: A relationship between mortality from chronic respiratory disease and some direct and indirect (e.g. fog frequency, urbanization) indices of air pollution was found. This relationship was shown in London (Hewitt, 1956; Burgess and Shaddick, 1959), in Salford near Manchester (Burn and Pemberton, 1963), in different areas in Great Britain (Pemberton and Goldberg, 1954; Daly, 1959; Stocks, 1959; Buck and Brown, 1964; Dean, 1966; Ashley, 1969; Gardner et al., 1969), and also in postmen (Fairbairn and Reid, 1958).

In a study in children a correlation was found between mortality from respiratory disease and some air pollution indices, particularly in the age group of less than one year (Collins et al., 1971).

Morbidity: Comparative studies of different areas varying in air pollution levels revealed higher prevalence rates for chronic respiratory disease in the more polluted areas (Fairbairn and Reid, 1958; Reid, 1962). After allowing for differences in smoking habits the same finding could be demonstrated

in a study in postoffice workers in London and three county towns (Holland and Reid, 1965), and in a postal survey in urban and rural areas (Lambert and Reid, 1970).

In a study of more than 2000 families in a suburb of London, Colley and Holland (1967) showed in the mothers and the children an effect of area of residence on the prevalence of winter cough, while in the fathers the prevalence of winter cough was related to smoking and social class.

In children several studies have demonstrated associations between long-term exposure to urban air pollution and the prevalence of non-specific respiratory disease and respiratory infections (Wahdan, 1964; Douglas and Waller, 1966; Lunn et al., 1967; Lunn et al., 1970). Colley and Reid (1970) found a consistent rise in the frequency of chest conditions with increasing local levels of air pollution clearly only among the children of semi-skilled and unskilled workers. A consistent and significant effect of area of residence on the prevalence of respiratory symptoms and on the peak expiratory flow rate was found by Holland et al. (1969, 1970) in schoolchildren in Kent. In a cohort study of children born in the last week of March 1946, Colley et al. (1973) found that at the age of 20 the prevalence of chronic cough was most affected by smoking cigarettes, while air pollution and social class had only little effect.

THE NETHERLANDS.

Mortality: Biersteker (1966) reported a higher mortality from chronic bronchitis in the Rotterdam born than in the Rotterdam import male population, possibly as a result of a longer exposure to air pollution.

Morbidity: Biersteker (1969) found no differences between male Municipal Employees in Rotterdam with symptoms of "bronchitis" and a group without these symptoms with regard to the number of years of residence in Rotterdam and in non-urban environments, and with regard to postal district address in Rotterdam. In a study comparing random samples of the population of the heavily polluted town of Vlaardingen and of the rural area of

Vlagtwedde, Van der Lende (1969) found in subjects aged 40-64 a relation between living in Vlaardingen and the prevalence of persistent cough and persistent phlegm, but not of dyspnoea. In men aged 15-39, Van der Lende et al. (1973^a) reported a relation between living in Vlaardingen and the prevalence of dyspnoea, especially in the cigarette smokers. This discrepancy in findings was contributed to a self-selection of the older age-groups in Vlaardingen. No effect of smoking or living in the polluted area on the lung function could be demonstrated. In comparative studies in children living in high and low polluted areas in the Netherlands a higher prevalence of respiratory symptoms was found in the more polluted areas (Kerrebijn et al., 1975; Biersteker et al., 1976). Biersteker et al. (1976) found also lower lung function values in the polluted area in their study, however previous studies by Biersteker and Van Leeuwen (1970) and by Kerrebijn (1975) did not reveal differences in lung function values.

4.3.1.2. UNITED STATES OF AMERICA.

Mortality: A relationship between long-term exposure to suspended particulate matter and mortality from chronic pulmonary disease among men aged 59-69 was demonstrated in a study comparing different parts of Buffalo and environs (Erie County); a relationship between long-term exposure to sulphates and mortality from chronic pulmonary disease was found only in the lowest two of the five economic levels used (Winkelstein et al., 1967, 1968).

Morbidity: In a study of a random sample of white women in Buffalo an association was shown between long-term exposure to suspended particulate matter and the prevalence of chronic cough and phlegm in non-smokers, and in smokers who had lived at the same place for at least five years (Winkelstein and Kantor, 1969).

No significant differences in school absenteeism from respiratory illnesses were found between schools located in different areas of Berlin, New Hampshire, with different pollution levels. However, differences were found in lung function values between

these schools which could be attributed to differences in air pollution exposure (Ferris, 1970).

In a longitudinal study in Berlin (New Hampshire), Ferris et al. (1971, 1973) found after standardizing for smoking habits lower prevalence rates of chronic respiratory disease and slightly higher lung function values in the second survey in 1967 as compared with the first survey in 1961, which could have been the result of reduced air pollution levels. However, this trend could not be confirmed in their survey in 1973 (Ferris et al., 1976).

In a comparative study in schoolchildren living in high and low polluted areas in Cincinnati, Chattanooga, and New York City, Shy et al. (1973) found a consistent relationship between impaired ventilatory function and exposure to SO₂ plus particulate matter.

Other comparative studies revealed a higher prevalence of respiratory symptoms (Chapman et al., 1973) and lower lung function values (Mostardie and Leonard, 1974) in the more polluted areas. Speizer and Ferris (1973^a, 1973^b) found in policemen that exposure to traffic pollution, but more so smoking, is a factor in the development of chronic respiratory disease; no effect of traffic pollution on the pulmonary function was found.

From a study in children and adults French et al. (1973) observed that exposure to air pollution of three years or longer was an important component in the increased risk for acute respiratory disease.

In contrast to the findings of the above mentioned studies Hrubec et al. (1973) found in twin pairs no effect of differences in exposure level to air pollution on the prevalence of respiratory symptoms, but they did find a strong effect of smoking. Also, Comstock et al. (1973) could not demonstrate differences in symptom prevalence and lung function values between telephone employees in urban and rural areas.

4.3.1.3. CANADA.

Morbidity: Bates (1967) reported fewer chest illnesses, less severe dyspnoea, and better lung function values in bronchitic

patients in Winnipeg as compared with similar patients in three other more polluted towns.

4.3.1.4. JAPAN.

Morbidity: Oshima et al. (1964) found in residents of the Tokyo-Yokohama area higher prevalence rates of chronic cough and phlegm, especially in the smokers, and lower lung function values as compared with a control group in a low polluted area.

4.3.2. INTERNATIONAL COMPARATIVE STUDIES.

4.3.2.1. GREAT BRITAIN / NORWAY.

Morbidity: In a study in male transport workers in Bergen, a non-polluted town in Norway, and in London, Mork (1962) found differences in the prevalence of chronic cough and phlegm that could be attributed to differences in smoking habits, but the differences in the prevalence of more serious symptoms of chronic non-specific lung disease and in ventilatory function could not be eliminated by standardizing for smoking habits, suggesting an additional effect of air pollution.

4.3.2.2. GREAT BRITAIN / UNITED STATES OF AMERICA.

Morbidity: In a study in post office and telephone workers in Great Britain and the USA, Holland et al. (1965) found higher prevalence rates of respiratory symptoms and lower lung function values in the British subjects, which could be attributed to the exposure to higher levels of air pollution.

In a migrant study Reid et al. (1966) found no differences in the prevalence of respiratory symptoms between British male migrants to America and native born Americans, which led to their hypothesis that removal to the USA was followed by a reduction in symptoms and resulted in an arrest in the progression of chronic non-specific lung disease.

4.3.3. SUMMARY.

From the few national mortality studies an association between mortality from chronic respiratory disease and some air pollution indices comes forward.

The national and international morbidity studies have demonstrated an effect of area of residence respectively air pollution on the prevalence of respiratory symptoms and lung function. This effect was most marked in smokers, particularly cigarette smokers. There is an indication that also social class plays a role.

It is not clear from these studies to what extent duration of exposure to urban air pollution is of importance.

4.4. SUMMARY OF THE EPIDEMIOLOGICAL STUDIES.

Studies on the effects of *short-term exposure* to high levels of urban air pollution have demonstrated an association between acute and subacute episodes of high pollution on the one hand and mortality and morbidity from respiratory disease on the other hand. One must keep in mind that it may be difficult to isolate the effect of air pollution from that of weather conditions.

No light has been shed on whether other factors, such as smoking habit and social class are of importance in this association.

Studies on the effects of *long-term exposure* to urban air pollution have shown an association between air pollution and morbidity from chronic respiratory disease, especially in cigarette smokers, in which other factors, such as socio-economical, may play a role. There is an indication of an association between air pollution and mortality from chronic respiratory disease.

CHAPTER III

GENERAL ASPECTS OF THE EPIDEMIOLOGICAL STUDY IN THE RIJNMOND AREA

1. INTRODUCTION.

The Rijnmond area is an area of 614 square kilometers at the mouth of the rivers Rijn and Maas with a population of just over one million in 1970. The geographical situation is shown in figure 3.1. This area is heavily polluted because of big oil refineries and other petrochemical industries along the south bank of the "Rotterdamse Waterweg", which runs from Rotterdam into the North Sea over a length of 30 kilometers and is formed by the "Nieuwe Maas", the "Scheur", and the "Nieuwe Waterweg". For many years the oil-fired central heating systems of the greenhouses in the "Westland" contributed also to the air pollution in this area but since a few years ago more and more of these central heating systems have changed from oil to natural gas which gives off far less pollution in its burning process.

One of the most polluted towns in this area is Vlaardingen situated to the west of Rotterdam on the north bank of the "Nieuwe Waterweg" opposite the petrochemical industrial complex. As the prevailing winds in the Netherlands are south and west Vlaardingen is frequently hit by polluted air from this complex.

Therefore, the population of Vlaardingen seemed to be very appropriate to study effects of air pollution on the airways in the Rijnmond area, and a severe air pollution episode occurring in the autumn of 1971 was the immediate cause to organize this present study which took place in 1973.

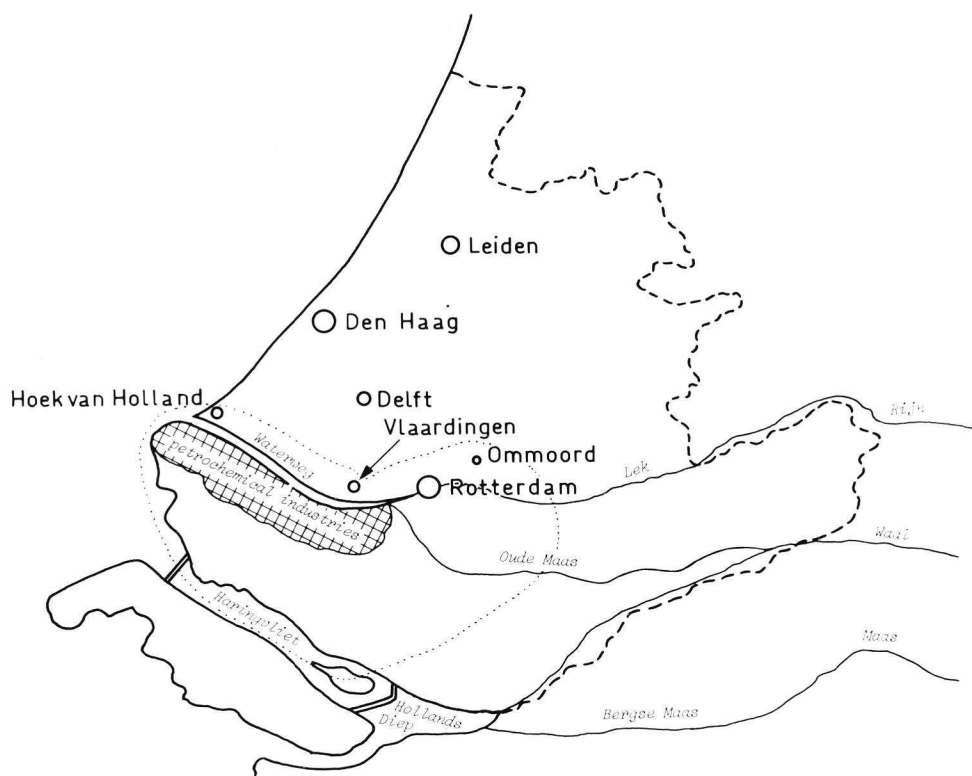


Fig. 3.1. The geographical situation of the Rijnmond area (shown by the dotted line).

2. ASPECTS OF THE AIR POLLUTION SITUATION IN THE RIJNMOND AREA.

As already mentioned the petrochemical industries on the south bank of the "Rotterdamse Waterweg" are the main source of air pollution in the Rijnmond area to which motor traffic and to a lesser extent the heating systems of the greenhouses also contribute.

To give an idea of the emissions by the petrochemical industries, it was estimated that per day about 680 tons of sulphur dioxide, 80 tons of nitrogen oxides, and 120 tons of hydrocarbons were emitted in the first three months of 1973 (Biersteker, 1975). However, the average pollution levels at ground level are relatively low in the Rijnmond area because of the very large chimneys used by the industries for their emissions. Some examples of the maximum daily air pollution levels measured in the Rijnmond area by the "Keuringsdienst van Waren" (Food Inspection Department), Rotterdam, in each quarter of the year 1973 are given in table 3.1.

Table 3.1. Maximum daily air pollution level of standard smoke, sulphur dioxide, nitrogen dioxide, and ozone, expressed in $\mu\text{g}/\text{m}^3$, measured at any measuring site in the Rijnmond area by the "Keuringsdienst van Waren", Rotterdam, in each quarter of the year 1973.

QUARTER OF THE YEAR	AIR POLLUTANT			
	standard smoke ¹⁾	sulphur dioxide ¹⁾	nitrogen dioxide ²⁾	ozone ³⁾
first	138	564	143	133
second	142	277	114	286
third	109	263	109	107
fourth	84	270	137	240

1) 24-hour samples; 28 measuring sites

2) 3-hour samples; 3 measuring sites

3) 1-hour samples; 2 measuring sites, but 1 in first quarter

(Source: Kwartaalverslagen, Laboratorium Luchtverontreiniging, Keuringsdienst van Waren, Rotterdam)

The severe air pollution episode that occurred in the Netherlands in the autumn of 1971 resulted in high air pollution levels in the Rijnmond area as well as in big cities elsewhere. However, only the population in the Rijnmond area complained of malodour and irritation of the airways, possibly as a result of the more complex mixture of hydrocarbons locally available, possibly as a result of coincidence of fumigations and smog formation on the same day now and then, possibly as a result of new chemical hazards due to mixing of sulphur dioxide and ozone (Biersteker, 1975). This latter hazard has recently been studied experimentally by Hazucha and Bates (1975).

3. GENERAL OUTLINE OF THIS EPIDEMIOLOGICAL STUDY IN RELATION TO CHRONIC NON-SPECIFIC LUNG DISEASE (CNSLD).

3.1. INTRODUCTION.

In designing this epidemiological study the following hypothesis on the basic mechanism involved in the effects of air pollution on the airways was considered: effects of air pollution on the airways can be assumed as being a consequence of having some degree of CNSLD. That is to say, air pollution is one of the non-specific exogenous stimuli which can cause respiratory symptoms and bronchial obstruction as a result of an existing hyperreactivity of the bronchus, which is one of the basic mechanisms in the aetiology of CNSLD (see figure 3.2.). In view of this hypothesis the general objectives of the study could be drawn.

3.2. OBJECTIVES OF THE STUDY.

The objectives of the study were as follows:

- a. to study whether there is an association between high levels of air pollution of short duration and an excess in respiratory morbidity, using respiratory symptoms and spirometric values as indices,
- b. to study whether persons with CNSLD differ from persons

- without CNSLD as regards a,
- c. to study which air pollutant might be responsible for the effects found.

3.3. GENERAL ASPECTS OF CNSLD.

3.3.1. DEFINITION OF CNSLD.

In order to improve the national and international comparability of the term CNSLD covering the clinical pictures of bronchial asthma, asthmatic bronchitis, chronic bronchitis, and emphysema strict diagnostic criteria have been developed gradually via various international conferences and symposia (CIBA, 1959; Orie and Sluiter, 1961; WHO, 1963; Orie and Sluiter, 1964; Orie and Van der Lende, 1970).

At present the term CNSLD is accepted as being applicable when at least one of the following symptoms is found: chronic or recurrent cough with expectoration, and paroxysmal or persistent excessive breathlessness, which are not solely attributable to a number of specified diseases (Fletcher, 1961). This description of CNSLD is based upon a standard questionnaire.

However, in order to qualify and compare the prevalence of CNSLD in populations it is preferable to apply a more detailed description of the respiratory symptoms and lung function impairments to take into account the severity of CNSLD (Van der Lende et al., 1973^b).

3.3.2. AETIOLOGY OF CNSLD.

Clinical and epidemiological studies have shown that exogenous factors such as smoking and various types of air pollution are of great importance in the development of CNSLD. From clinical studies (Orie et al., 1961), and later from epidemiological findings (Van der Lende, 1969; Van der Lende et al., 1970) it gradually emerged that also endogenous factors, such as age, sex, tendency to allergy, and bronchial hyperreactivity, could have a substantial share in the aetiology of CNSLD.

The development of the final clinical manifestation of CNSLD can be hypothesized as is shown in figure 3.2.

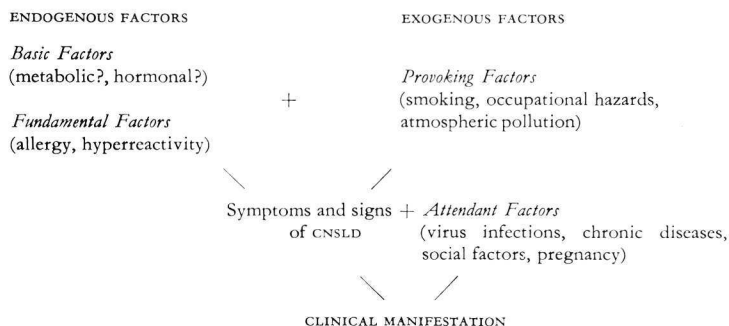


Fig. 3.2. The role of various factors in the development of CNSLD.

(Reproduced from *Bronchitis III*, p. 55, edited by Orie, N.G.M. and Van der Lende, R., 1970, by permission of the publishers, Royal VanGorcum, Assen)

3.4. DISTURBING FACTORS IN THE STUDY ON THE EFFECTS OF AIR POLLUTION ON THE AIRWAYS.

As the present epidemiological study is concerned with the effects of air pollution on the airways it is of importance in view of the aetiological hypothesis to minimize as far as possible disturbing influences of other exogenous factors, and of endogenous and attendant factors.

In order to achieve this the population under investigation was matched to a control population living under the same meteorological conditions as could be assumed. The matching variables were sex, age, smoking habit, and degree of CNSLD, on which information was gained by using the TNO questionnaire on respiratory symptoms. By studying only women it was tried to avoid occupational hazards and to reduce smoking influences.

No conclusive information on the attendant factors was gained, firstly because some of these factors would be fairly constant throughout the period of observation, secondly because others would be very difficult to objectify in this type of study.

CHAPTER IV

METHODS OF INVESTIGATION

1. INTRODUCTION.

The study was carried out in a sample of the female population in Vlaardingen aged 18-42 years, which was divided into four groups according to the degree of CNSLD. This grouping was based upon the answers to a standard questionnaire on respiratory symptoms and upon spirometric values. As control population women in Ommoord - a relatively low polluted district of Rotterdam - were chosen who were sampled by individual matching. During the year of investigation a day by day follow-up of respiratory symptoms was assessed by using a diary technique. Lung function measurements were done weekly during home visits by trained staff. Air pollution and meteorological data were collected in both areas.

In this Chapter the subsequent methods will be discussed.

2. QUESTIONNAIRE ON RESPIRATORY SYMPTOMS.

For obtaining and comparing anamnestic data in epidemiological studies on respiratory disease (as well as on other diseases) the use of a standard questionnaire by trained interviewers is one of the essentials (Holland et al., 1966; Van der Lende, 1969; Van der Lende and Orie, 1972). For this purpose the first standard questionnaire on respiratory symptoms was devised by the Medical Research Council (MRC) in Great Britain in 1960. After practical experience this prototype was slightly revised in 1966. A special working group of the European Coal and Steel Community (ECSC) brought out a questionnaire in 1961 and in

1967. Both questionnaires were mainly based upon the MRC-questionnaire (Minette et al., 1967).

The TNO Research Unit for Epidemiology of CNSLD of the Dutch Organization for Health Research TNO use in their investigations the TNO-questionnaire on respiratory symptoms which is as comparable with the MRC- and ECSC-questionnaire as could be achieved. A copy of the complete questionnaire is given in Appendix B-1.

The population in this study was subdivided into four groups according to the degree of CNSLD based upon the answers to the TNO-questionnaire and upon the $FEV_{1.0}$ expressed as percentage of the VC as follows:

- grade 0: no indication of CNSLD: no respiratory symptoms and no impairment of the lung function, i.e. $FEV_{1.0}\%VC$ not more than 10% below the predicted value;
- grade 1: slight degree of CNSLD: slight respiratory symptoms and no impairment of the lung function;
- grade 2: moderate degree of CNSLD: moderate respiratory symptoms and/or slight to moderate impairment of the lung function, i.e. $FEV_{1.0}\%VC$ 10-20% below the predicted value;
- grade 3: severe degree of CNSLD: severe respiratory symptoms and/or moderate to severe impairment of the lung function, i.e. $FEV_{1.0}\%VC$ more than 20% below the predicted value.

The diagnostic criteria of the different grades of CNSLD were made specially for the requirements of this study. Full details on these criteria are given in Appendix B-2. Later Van der Lende et al. (1975^b) published a further refinement of these criteria for general use in epidemiology of CNSLD.

3. SPIROMETRY.

The vital capacity and the forced expiratory volume in one second were obtained in both populations by means of the LODE Spirograph D 53, which is a water-sealed spirometer and which

meets the standards set by the ECSC (Cara et al., 1961). The inspiratory vital capacity was recorded and immediately after this manoeuvre a forced expiratory volume in one second was recorded. The best values for VC and FEV_{1.0} of at least three manoeuvres were registered at ambient temperature and pressure saturated with water vapour (ATPS). The advantage of this type of spirometer is that it has a low inertia and resistance of the measuring system, that the inspiratory and expiratory manoeuvres are written on a chart and that the curves can be checked immediately for correctness.

4. POPULATION.

4.1. POPULATION IN VLAARDINGEN.

In 1969 the TNO Research Unit for Epidemiology of CNSLD conducted a survey in a random sample of the population in Vlaardingen aged 15-39 years taken from the Civil Registry. Of the 1590 persons who took part in the survey 795 were women. In 1972 a follow-up study was carried out. Between 1969 and 1972 135 women were lost (134 women moved and 1 woman died) leaving 660 women to take part in this second survey. According to the mentioned diagnostic criteria these women were subdivided into the four grades of CNSLD. Of these 660 women 536 (81.2%) were willing to take part in this study, the age range now being 18-42 years. Table 4.1. shows that there is only a slight difference between the percentages of women who were willing to take part in the different grades of CNSLD, which proved not to be significant using a chi-square test on a 2 x 4 contingency table ($0.1 < P < 0.2$). So there is no indication that the willingness to take part in the study has been influenced by degree of CNSLD.

As the data of the 1972-survey were not available in time to be used in the organization of this study, the subdivision of the women into the four groups according to the degree of CNSLD was based upon the answers to the questionnaire taken in 1969 and upon the spirometric values from that survey.

Table 4.1. Percentage of women who were willing to take part in the study according to degree of CNSLD.

DEGREE OF CNSLD	NUMBER OF WOMEN IN 1972 LEFT FROM THE SURVEY IN 1969	NUMBER OF WOMEN WILLING TO TAKE PART IN THIS STUDY	
	N	N _t	%
grade 0	316	252	79.4
grade 1	193	163	84.5
grade 2	141	115	81.6
grade 3	10	6	60.0
Total	660	536	81.2

The total number of 536 women who were willing to take part outnumbered the number of about 400 women that was set as a total that could be included in the study with regard to manpower and finances. Consequently, a reduction had to be made and that only in the subgroups grade 0 and 1 because of their numbers. This was done by drawing lots. After drawing lots the numbers were as follows: 150 women in grade 0, 155 women in grade 1, 115 women in grade 2, and 6 women in grade 3, making up a total of 426 women. However, in the matching procedure 30 women had to be left out (see section 4.3.) so the definitive Vlaardingen population that entered the study consisted of 396 women and was subdivided as follows:

grade 0: 150 women,
grade 1: 128 women,
grade 2: 112 women,
grade 3: 6 women.

4.2. POPULATION IN OMMOORD.

In Ommoord the vast majority of the inhabitants of this district of Rotterdam are registered with the Health Centre's group practice of six general practitioners. In 1972 it was found that the registers of this group practice had 3020 women in the age group 18-42 years. All of these women were sent a letter out-

lining the study very briefly and asking whether they were willing to take part.

Enclosed was a very short questionnaire containing the major six questions on respiratory symptoms of the TNO-questionnaire in order to obtain an estimate of the number of women in each grade of CNSLD.

The short questionnaire was as follows:

- Question 1. Do you usually cough during the day -or at night- for as much as three months each year?
2. Do you usually bring up phlegm during the day -or at night- for as much as three months each year?
 3. In the past three years have you had a period of cough and phlegm lasting for three weeks or more?
 4. Are you troubled by shortness of breath when walking up a staircase?
 5. Does your chest ever sound wheezing?
 6. Have you ever had attacks of shortness of breath with wheezing (asthmatic attacks)?

The criteria for a provisional grading were:

grade 0: negative answers to all questions,

grade 1: one or two positive answers to the questions 1-5, and a negative answer to question 6,

grade 2: three to five positive answers to the questions 1-6,

grade 3: positive answers to all questions.

Of the 1169 women who replied 1048 women were willing to take part in the study. The provisional grading of these 1048 women was as follows: 604 women in grade 0, 332 women in grade 1, 102 women in grade 2, and 10 women in grade 3.

In the provisional grade 0 group in Ommoord the age distribution differed from that in the original sample in grade 0 in Vlaardingen. In view of the future matching it was decided to take a sample per age group by drawing lots in order to equalize as far as possible the numbers in the different age-groups in both subgroups grade 0. (See table 4.2.).

Table 4.2. Age distribution of the women in subgroup grade 0 according to area of residence.

AGE	NUMBER OF WOMEN IN GRADE 0							
	IN VLAARDINGEN			IN OMMOORD				
	in original sample			willing to take part			after drawing lots	
	N _t = 316			N _t = 601 ¹⁾			N _t = 309	
	n	%		n	%		n	%
18-24 yrs	122	38.6		115	19.2		115	37.2
25-30 yrs	65	20.6		210	34.9		65	21.0
31-36 yrs	63	19.9		143	23.8		63	20.4
37-42 yrs	66	20.9		133	22.1		66	21.4

¹⁾ age unknown in 3 of the 604 women.

Still only a provisional grading was known in the Ommoord population consisting now of a total of 753 women. In order to arrive at a definitive grading according to the grading criteria used in Vlaardingen additional investigation was needed. Of the 753 women called for further investigation 626 women turned up. Apart from lung function tests and X-ray examination, the women were asked a few personal questions particularly on having a job. This revealed that 488 women were living *and* staying most days of the week in Ommoord. Then it was tried to visit these 488 women at home in order to take the TNO- questionnaire on respiratory symptoms. This was done by two trained health visitors. In total 463 women could be interviewed and according to the mentioned diagnostic criteria they could be subdivided as follows: 184 women in grade 0, 137 women in grade 1, 131 women in grade 2, 11 women in grade 3. When matched pairs were formed some of the women had to be left out and the definitive numbers in each grade of CNSLD were consequently equal to those in Vlaardingen, namely:

grade 0: 150 women,
grade 1: 128 women,

grade 2: 112 women,
grade 3: 6 women.

4.3. MATCHING.

To eliminate the effects of factors that may confound the analysis of study variables the method of individual matching (MacMahon and Pugh, 1970) was applied.

The factor CNSLD - apart from being a study variable - was considered to be also a confounding factor, because different prevalences of CNSLD in the populations under investigation as well as a possible different reaction pattern of the subjects in the different grades of CNSLD to exposure to air pollution could influence the results.

The other confounding factors in this study were thought to be smoking habit and age.

The criteria used for the classification of the subjects in the grades of CNSLD are already described above. The smoking habit was categorized as follows: present smoker, non-smoker, and ex-smoker (i.e. stopped smoking for at least one month) using the data from the questionnaires taken in 1972. With regard to age it was tried to match on the years of age per the first of October 1972, or, if this could not be achieved, as close as possible with a maximum age-difference of five years.

To each individual of the study population a control was selected with respect to degree of CNSLD, smoking habit, and age. The matching procedure is tabulated in table 4.3.

As can be seen from this table 30 women in Vlaardingen were lost because no suitable control could be found either because of a shortage of controls in the subgroups or because no matching on age could be achieved.

Consequently 396 pairs of women entered the study.

It should be mentioned here that a disadvantage of applying this method is that when data of a control are missing during one or more periods of the investigation the data of the partner are also of no value during that time.

Table 4.3. Schematized matching procedure of the women in Vlaardingen and Ommoord on degree of CNSLD, smoking habit, and age.

DEGREE OF CNSLD	SMOKING HABIT	NUMBER OF WOMEN				NUMBER OF MATCHED PAIRS
		AVAILABLE FOR MATCHING		LOST IN PROCEDURE		
		Vl.	Om.	Vl.	Om.	
grade 0	non-smoker	69	81	0	12	69
	smoker	65	69	0	4	65
	ex-smoker	16	34	0	18	16
grade 1	non-smoker	52	51	3	2	49
	smoker	86	63	24	1	62
	ex-smoker	17	23	0	6	17
grade 2	non-smoker	31	40	0	9	31
	smoker	72	71	3	2	69
	ex-smoker	12	20	0	8	12
grade 3	non-smoker	3	4	0	1	3
	smoker	3	7	0	4	3
	ex-smoker	0	0	0	0	0
Total		426	463	30	67	396

5. CONDUCT OF THE SURVEY.

5.1. DIARY TECHNIQUE.

In order to assess the daily prevalence of respiratory symptoms a diary technique was applied. The diary was specially designed for this study, and in figure 4.1. a copy of a diary page is shown.

For each day of the week questions were asked about the absence or presence of respiratory symptoms i.e. coughing, phlegm, dyspnoea, and wheezing, and of eye-irritation. Although this latter symptom is not a respiratory one it was introduced because it is often encountered in periods of photochemical smog.

The questions had to be answered by ticking either the NO-column or the YES-column. The YES-column was subdivided into the following five possibilities represented in a code:

-- = much less than usual
- = less than usual
0 = as usual¹⁾
+ = more than usual
++ = much more than usual

1) as usual referred to the presence of a symptom for at least five days of the week.

The home visitors handed out the diaries to the women and instructed them personally. Besides, in each diary was a separate sheet with directions for use and a few examples. Every three months new diaries were handed out to minimize the risk of loosing data. To make a change for the women, the diaries had a special coloured cover for each season.

The subjective data gained in this way were thought to be very valuable with respect to the objectives of this study, because Lawther et al. (1970) reported that the results of their diary studies proved useful in assessing the relative importance of pollution and weather in producing exacerbations of "bronchitis".

5.2. HOME VISITS.

In addition to the subjective data collected by means of diaries, the lung function - as an objective parameter - was measured weekly at the women's homes (see section 5.3.). The home visits were made by trained female staff and organized in such a way that each person was visited weekly on the same time of the same day by the same home visitor, and that the members of a matched pair were visited on the same day of the week. A scheme for the visits was made at random in Vlaardingén. If for some reason a person wished to be visited on another day of the week, the home visit of her partner switched also to that day of the week. An added advantage of these home visits was the possibility to check whether the diary was filled in properly during the previous week and to collect phlegm that was

REMARKS

Week

	NO	YES				
		--	-	0	+	++
SUNDAY						
Cough	☐	☐	☐	☐	☐	☐
Phlegm	☐	☐	☐	☐	☐	☐
Dyspnoea	☐	☐	☐	☐	☐	☐
Wheezing	☐	☐	☐	☐	☐	☐
Eye-irritation	☐	☐	☐	☐	☐	☐
MONDAY						
Cough	☐	☐	☐	☐	☐	☐
Phlegm	☐	☐	☐	☐	☐	☐
Dyspnoea	☐	☐	☐	☐	☐	☐
Wheezing	☐	☐	☐	☐	☐	☐
Eye-irritation	☐	☐	☐	☐	☐	☐
TUESDAY						
Cough	☐	☐	☐	☐	☐	☐
Phlegm	☐	☐	☐	☐	☐	☐
Dyspnoea	☐	☐	☐	☐	☐	☐
Wheezing	☐	☐	☐	☐	☐	☐
Eye-irritation	☐	☐	☐	☐	☐	☐
WEDNESDAY						
Cough	☐	☐	☐	☐	☐	☐
Phlegm	☐	☐	☐	☐	☐	☐
Dyspnoea	☐	☐	☐	☐	☐	☐
Wheezing	☐	☐	☐	☐	☐	☐
Eye-irritation	☐	☐	☐	☐	☐	☐
THURSDAY						
Cough	☐	☐	☐	☐	☐	☐
Phlegm	☐	☐	☐	☐	☐	☐
Dyspnoea	☐	☐	☐	☐	☐	☐
Wheezing	☐	☐	☐	☐	☐	☐
Eye-irritation	☐	☐	☐	☐	☐	☐
FRIDAY						
Cough	☐	☐	☐	☐	☐	☐
Phlegm	☐	☐	☐	☐	☐	☐
Dyspnoea	☐	☐	☐	☐	☐	☐
Wheezing	☐	☐	☐	☐	☐	☐
Eye-irritation	☐	☐	☐	☐	☐	☐
SATURDAY						
Cough	☐	☐	☐	☐	☐	☐
Phlegm	☐	☐	☐	☐	☐	☐
Dyspnoea	☐	☐	☐	☐	☐	☐
Wheezing	☐	☐	☐	☐	☐	☐
Eye-irritation	☐	☐	☐	☐	☐	☐

-- much less than usual
- less than usual
0 as usual
+ more than usual
++ much more than usual

Week number	☐	Lung function	☐
Visitor	☐		☐
Day of visit	☐		☐
Hour of visit	☐		☐

Fig. 4.1. Copy of a diary page.

brought up in the first hour after getting up on the day of the visit (see section 5.4.).

Apart from gaining data the home visits were considered to be very important as a stimulus to arrive at an optimum cooperation of the women, especially because Lawther et al. (1970) found that people lose interest in keeping a day by day record of their symptoms, particularly when they do not have complaints.

5.3. LUNG FUNCTION MEASUREMENTS.

Lung function measurements were carried out with a portable spirometer. For this purpose the Monaghan Pulmonary Function Analyzer Model M403 was chosen as it appeared at first instance very reliable and suitable. This electronic spirometer has a thermistor wire in its mouthpiece which is held at a constant temperature of 200-220° centigrades. When an airflow goes across this thermistor the temperature tends to decrease and the voltage needed to keep the thermistor at constant temperature is proportional to the flow rate. The flow is integrated over time to give volume. The device is calibrated for air saturated with water vapour at 37° centigrades.

A clinical evaluation of this spirometer showed no significant difference in FVC and FEV_{1.0} as compared with a Collins 13.5 liter water-sealed spirometer (Cox et al., 1973).

A total of six Monaghan spirometers were made available for this study by SANDOZ, Uden, the Netherlands (the representatives of The Monaghan Company, Denver, Colorado), so that each member of the visiting team had one Monaghan spirometer and the serial weekly lung function tests were done with the same instrument in the same individuals.

The instruments were used as calibrated by the factory. However, the instruments were gauged at intervals to allow for differences between instruments. This gauging was done on the peak expiratory flow rate connecting the inflow side of the mouthpiece to the Godard rotameter, using calibrated flows from 135 to 600 liters per minute. After performing a forced expiratory manoeuvre the FVC, FEV_{1.0}, and PEF (Peak Expiratory Flow) can be read immediately by pressing the respective push-

button. In this study at least three forced expiratory manoeuvres were done. The values for FVC and $FEV_{1.0}$ were taken from the reading with the best $FEV_{1.0}$ and noted in the diary. At the end of each day the mouthpiece was cleaned as deposits of particles on the thermistor affects its proper functioning. However, during the first months of the survey the instruments proved to be liable to electrical disturbances and failures presumably because they were carried around and switched on and off very often. Therefore, after three months the Wright Peak Flow meter was also introduced because this instrument was proven to be suitable and reliable in epidemiological studies (Tammeling et al., 1969). Each home visitor had one Peak Flow meter and these meters were also gauged at intervals for flow as described with respect to the Monaghan spirometer. It was hoped that weekly lung function measurements could attribute to the objectives of the study as it was organizationally impossible to do measurements more frequently during the week. It is however possible that the weekly lung function values would not shed a light on an association between lung function and air pollution.

5.4. SPUTUM COLLECTION.

The home visits being organized gave a good opportunity to collect phlegm as well, if any. At the start of the survey the women were handed out little sterile sputum jars which could contain up to 50 ml., and were asked to collect phlegm that was brought up in the first hour after getting up on the day of the home visit. In case any phlegm was brought up the respective women received clean jars.

The home visitors estimated the volume, made a judgement on the macroscopic aspect i.e. mucous, muco-purulent, or purulent, and noted the results in the diary.

In this way it was attempted to check whether an agreement existed between the answer on the question on phlegm production and the handing in of sputum on the day of the home visit, and to determine to what degree intercurrent bacterial respiratory infections occurred.

6. AIR POLLUTION DATA.

In Vlaardingen - being one of the most polluted towns in the Rijnmond area - four official bodies had air pollution monitoring stations in operation in 1973, namely the "Dienst Centraal Milieubeheer Rijnmond", the "Keuringsdienst van Waren", the "Rijksinstituut voor de Volksgezondheid", and "TNO". Most of the Vlaardingen data needed were kindly supplied by these bodies to the TNO Research Institute for Environmental Hygiene. The few remaining lacking data were additionally measured by this Institute.

In Ommoord there was only one station measuring sulphur dioxide and standard smoke (by the "Keuringsdienst van Waren"). Therefore, the "Rijksinstituut voor de Volksgezondheid" specially set up a monitoring station in the top floor of the Health Centre in Ommoord to supplement the lacking information.

All data collection and data reduction for ozone and nitrogen oxides was done by "TNO".

The following air pollutants were measured and used as indicators of the general level of pollution in the area in order to try and find an association between air pollution and respiratory symptoms and lung function values: sulphur dioxide, standard smoke, nitrogen oxides, ozone, and aldehydes. Initially sulphuric acid and hydrocarbons were also intended to be included, but measurements on these pollutants could not be carried out because of technical reasons.

The air pollution data of special interest for this study were daily average and daily maximum values, with the essential requirement that the data in Vlaardingen and Ommoord would be comparable.

Sulphur dioxide was measured 24-hourly and 1-hourly. The 24-hourly method of measuring SO_2 was based on absorption in a dilute hydrogen peroxide solution, followed by acid titration, which is a standard OECD (Organization for Economic Cooperation and Development) method (OECD, 1964). The 1-hourly measurements of SO_2 were done by an SO_2 measuring instrument made by Philips, Eindhoven, the Netherlands, and the method was based upon a

coulometric¹⁾ principle.

In Vlaardingen the 1-hourly values were produced automatically and the mean value of the data received from seven measuring stations was calculated. If at a particular station more than seven 1-hourly values were missing, then the day's data from that station were considered as missing. If data from more than one station were missing, no values for that day were given. In Ommoord SO₂ 1-hourly values had to be read manually from the graph on a strip chart recorder. Unfortunately failures in registration on the strip chart recorder occurred and consequently all these data had to be considered as inaccurate.

Standard smoke was measured 24-hourly. This was done by means of reflectometry²⁾ on standard filter paper (standard OECD method).

Nitrogen oxides and *ozone* were measured 1-hourly. The concentrations of these pollutants were measured by means of automatic measuring instruments made by Enraf Nonius, Delft, the Netherlands, based on colorimetric³⁾ principles. Whether day's data were missing was decided by the same procedure as was used for the 1-hourly SO₂ values.

Aldehydes were measured 24-hourly and 8-hourly separately by the MBTH method (methyl benzothiazolone hydrazone) (Hauser and Cummins, 1964).

The concentrations of aldehydes as found in Ommoord in the first six months of the survey were thought to be caused by - as it later appeared - the recently tarred roof of the Health Centre from which aldehydes were liberated especially during warm and

1) Coulometry: chemical analysis performed by determining the amount of a substance released in an electrolysis by measuring the number of coulombs used. The coulomb is the practical SI unit of electric charge equal to the quantity of electricity transferred by a current of one ampère in one second.
SI: Système International d'Unités.

2) Reflectometry: method of measuring the reflectance of radiant energy.

3) Colorimetry: chemical analysis by comparison of a liquid's colour with standard colours.

Table 4.4. The air pollution data collected in Vlaardingen and Ommoord which were used in the analysis.

AIR POLLUTANT	DURATION OF SAMPLING	DATA USED IN THE ANALYSIS	OFFICIAL BODY WHO'S MONITORING STATION SUPPLIED THE DATA
Sulphur dioxide	24 hours	24-hour average	Keuringsdienst van Waren (Food Inspection Department)
Standard smoke	24 hours	24-hour average	Keuringsdienst van Waren (Food Inspection Department)
Nitrogen monoxide	1 hour	daily average daily maximum	Rijksinstituut voor de Volksgezondheid (National Institute of Public Health)
Nitrogen dioxide	1 hour	daily average daily maximum	Rijksinstituut voor de Volksgezondheid (National Institute of Public Health)
Ozone	1 hour	daily average daily maximum	Rijksinstituut voor de Volksgezondheid (National Institute of Public Health)
Aldehydes	24 hours	24-hour average	TNO Instituut voor Milieuhygiene en Gezondheidstechniek (TNO Research Institute for Environmental Hygiene)
Aldehydes	8 hours (8.00 a.m.- 4.00 p.m.)	8-hour average	TNO Instituut voor Milieuhygiene en Gezondheidstechniek (TNO Research Institute for Environmental Hygiene)

sunny spells. Consequently, the data on ozone were probably also unreliable. Therefore, during the second half of the survey air was sampled from another spot of the building to measure aldehydes and ozone.

In table 4.4. the air pollution data collected in Vlaardingen and Ommoord which were used in the analysis are summarized.

7. METEOROLOGICAL DATA.

As it was assumed that Vlaardingen and Ommoord were exposed to similar meteorological conditions an attempt was made to objectify this. In both areas daily maximum and minimum values were collected on temperature and relative humidity i.e. the ratio of quantity of water vapour present in the atmosphere to the quantity of water vapour which would saturate at the existing temperature. The measurements on temperature and on relative humidity were carried out in cooperation with the KNMI (Royal Dutch Meteorological Institute) which kindly lent the TNO Research Institute for Environmental Hygiene two thermographs and two hygrographs to be placed in Vlaardingen and Ommoord.

CHAPTER V

PRESENTATION OF THE DATA AND METHODS OF STATISTICAL ANALYSIS

1. INTRODUCTION.

The way this study was set up - a study population matched to a control population - constrains an analysis of *differences* in daily symptom prevalence and weekly peak flow values between the population in Vlaardingen and Ommoord. The subjects in the groups CNSLD grade 0 (no CNSLD) and grade 1 (slight degree of CNSLD) in Vlaardingen were subsampled from the original sample (see Chapter IV, section 4.1.), so that the final sample should be considered as a stratified sample from the Vlaardingen women aged 18-42 years. Because the group CNSLD grade 3 consisted of only three pairs of women, it was decided to combine the categories CNSLD grade 2 and grade 3 (moderate and severe degree of CNSLD) in the analysis as no reductions were made in their original samples.

To look for a possible association between high air pollution levels and affection of the airways, the differences in symptom prevalence and lung function values between the Vlaardingen and Ommoord members of the pairs on days when the air pollution levels were high in Vlaardingen and low in Ommoord were compared with the differences on days when the reverse occurred. To take into account a possible manifestation of effects shortly after a high pollution level had occurred, the analysis was also carried out using a time lag of one day and two days.

The methods which were applied in selecting these days of which the data obtained in the population were analyzed are described

in section 3.2. of this Chapter.

2. PRESENTATION OF THE DATA.

2.1. DIARIES.

For each question in the diary a scoring system was made ranging from 0 to 5 as follows:

Answer	Score
NO	0
YES: much less than usual	1
less than usual	2
as usual	3
more than usual	4
much more than usual	5

In using this scoring system the answers in the diary were given a weight which will reflect the severity of a symptom present on that particular day.

For each day the difference in score of the Vlaardingen member minus the Ommoord member of each pair was taken for each symptom. Next, for each day the mean of these score-differences in all pairs within each CNSLD category was calculated for each symptom. These daily means are plotted in the figures C 1 to 5 in Appendix C. In the TABLES C-1.1. to C-5.3. the actual values of the data presented in these figures are given, and also the number of pairs from which the data were obtained.

2.2. LUNG FUNCTION MEASUREMENTS.

As has already been mentioned in Chapter IV, section 5.3., the Monaghan electronic spirometer M403 is probably not the most suitable instrument for this type of investigation. The lung function values obtained in a person on a number of successive weeks with the same Monaghan spirometer and by the same observer showed rather large fluctuations. In a comparison of the

peak flow values¹⁾ measured with the Monaghan spirometer and the Wright Peak Flow meter large differences were also observed. Based upon 1834 pairs of values obtained during 22 weeks by the same observer and with the same Monaghan spirometer and Wright Peak Flow meter, an estimated correlation coefficient of 0.69 was derived, which was thought to be very low for parallel measurements. If, based upon these 1834 pairs of observations, a linear prediction formula is derived (using the Wright peak flow value to predict the Monaghan peak flow value) the estimated standard deviation of the error is as high as 59.7 l/min. Consequently, the Monaghan measurements were found insufficiently reliable and it was thought best to abstain from the data obtained with the Monaghan spirometer and to analyze only the data obtained with the Wright Peak Flow meter.

The following method of analyzing the peak flow values was applied to relativize the absolute differences, which are for example influenced by the individual's height.

For each member of a pair the mean of all weekly peak flow values was calculated. Next, the difference between each single observation and the calculated mean in a person was formed, and finally, the ratio of this difference and the calculated mean was determined ("relative deviation from the mean", or "percentage difference from the mean"). Then for each pair the difference in this percentage of the Vlaardingen member minus the Ommoord member was taken for each day of the year that peak flow values were obtained in both members. Of the *pairs* who performed a lung function test on a same day the mean of the differences in "percentage difference from the mean" was determined for that day, according to degree of CNSLD.

In figure C 6 in Appendix C these daily means are plotted, of which the actual values are given in the TABLES C-6.1. to C-6.3. It should be mentioned that no lung function tests were carried out on Saturdays and Sundays, and that by the circumstances the

¹⁾ Normal peak flow values in healthy adult females range from about 300 to 500 liters/min., depending on height.

peak flow values measured by means of the Wright Peak Flow meter were only available from day 92 onwards, providing data on in total 165 days.

2.3. AIR POLLUTION DATA.

The following air pollution data -which were available both in Vlaardingen and Ommoord- were used in the analysis: concentrations of sulphur dioxide (24-hour averages), standard smoke¹⁾ (24-hour averages), nitrogen monoxide (daily averages and maxima), nitrogen dioxide (daily averages and maxima), ozone (daily averages and maxima), and aldehydes (8-hour and 24-hour averages). In the figures D 1 to 10 in Appendix D these data expressed as micrograms per cubic meter are plotted according to area of residence for each air pollutant separately. The actual values which correspond with the graphs are given in the TABLES D-1. to D-10.

As mentioned in Chapter IV, section 6., the daily maximum values of sulphur dioxide during the whole year, and the data on ozone and aldehydes during the first six months in Ommoord were too unreliable to take into account in the analysis. Consequently, these data obtained in Vlaardingen had also to be left out in the analysis.

2.4. METEOROLOGICAL DATA.

The data on temperature (daily maxima and minima) and on relative humidity (daily maxima and minima) that were collected in Vlaardingen and Ommoord are plotted for the year of investigation according to area of residence in the figures E 1 to 4 in Appendix E. The actual values which correspond with the graphs are given in the TABLES E-1. to E-4.

¹⁾ The method of measuring smoke by means of standard paper filters gives lower readings than when using fibreglass filters.

3. METHODS OF STATISTICAL ANALYSIS.

3.1. INTRODUCTION.

The matched pairs in each category of CNSLD are considered as being a random sample of the total population of possible pairs of women in the age-group 18-42 years in that category of which the one member lives in Vlaardingen and the other in Ommoord. Because of the applied method of individual matching no allowance had to be made for differences in age and smoking habit between the members of a pair.

It was tested whether or not the prevalence (severity) of the symptoms was higher and whether or not the peak flow values were lower on days with high air pollution levels than on days with low air pollution levels. This was done in each CNSLD category (grade 0, 1, and 2+3) for each smoking category (smokers, non-smokers, and ex-smokers), so for nine "CNSLD-smoking cells" separately. Within each CNSLD category the same test was applied to all smoking categories combined, and within each smoking category to all CNSLD categories combined. Finally, the same test was applied to all nine CNSLD-smoking cells combined. A test on a combination of categories was applied since it may reveal an "effect" which is present in all composing categories but not strong enough to yield a significant result when tested in the categories separately. If in any combined problem a significant result was found, it was tested whether the "effects" differed between separate categories.

3.2. THE SELECTION OF THE DAYS FOR THE ANALYSIS.

As already mentioned in the Introduction of this Chapter, one or more days had to be selected when levels of air pollution were high in Vlaardingen and low in Ommoord, and analogously one or more days when levels of air pollution were low in Vlaardingen and high in Ommoord.

As the levels of the individual air pollutants are used as indicators of the general level of air pollution, days were

selected for each air pollutant separately. Three methods (A, B, and C) were used in the selection procedure, yielding for each air pollutant a set of selected days in category A, B, or C depending on the method. The categories A and B served for the analysis of the data on the symptoms. Category B was introduced, because - according to method A - some extremely polluted days in Vlaardingen would otherwise have been excluded from the analysis. Category C served for the analysis of the data on the peak flow measurements.

The selection was carried out by means of percentiles¹⁾ of concentration values measured during the year of 1973, computed for the individual air pollutants in Vlaardingen and Ommoord separately.

The methods of selecting days were for each air pollutant:

Method A, selecting days with "high pollution levels"

(Category A):

1. the concentration in Vlaardingen being above the 95th percentile of Vlaardingen and the concentration in Ommoord equal to or below the 70th percentile of Ommoord being at least 25% below the concentration in Vlaardingen;
2. the concentration in Ommoord being above the 95th percentile of Ommoord and the concentration in Vlaardingen equal to or below the 70th percentile of Vlaardingen being at least 25% below the concentration in Ommoord.

Method B, selecting days with "peak pollution levels"

(Category B):

1. the concentration in Vlaardingen being above the 99th percentile of Vlaardingen and the concentration in Ommoord at least 25% below the concentration in Vlaardingen;
2. the concentration in Ommoord being above the 99th percentile of Ommoord and the concentration in Vlaardingen at least 25% below the concentration in Ommoord.

1) Percentile: a value which is taken such that a certain percentage of a set of values is below or equal to it.
Thus, for example, the 95th percentile means 95 percent of the observations is below or equal to the 95th percentile.

Method C, selecting two days (see section 3.4.) from category A or B (Category C):

1. the concentration in Vlaardingen being highest;
2. the concentration in Ommoord being highest.

The days in category C were selected from day 92 onwards, excluding Saturdays and Sundays, as otherwise no peak flow values were available.

In addition to these criteria it was required that in each category a time interval of at least three days existed between the days in group 1. and the days in group 2., in view of a possible ebbing or lagging of "effects".

Because of this possibility the analysis described in the sections 3.3. and 3.4. was also carried out for the days that are *one* day later than those in category A, B, and C, and for the days that are *two* days later than those in these categories.

3.3. TESTING THE INFLUENCE OF AIR POLLUTION ON RESPIRATORY SYMPTOMS AND IRRITATION OF THE EYES.

The analysis described in this section was performed for the selected days in category A as well as for the selected days in category B. Whenever "selected days" are mentioned in this section, either those in category A or in category B are meant. Because matched pairs were used in the investigation, only differences in scores of a respiratory symptom or irritation of the eyes between the members of a pair are considered, disregarding the scores of the separate members of a pair. The score of the Vlaardingen member minus the score of the Ommoord member of one pair on a particular day will in the following be denoted by the "score-difference".

In testing the influence of a high level of an air pollutant on a certain respiratory symptom or on the irritation of the eyes, for each pair the mean score-difference was calculated over the selected days with a high level in Vlaardingen. The same was done over the selected days with a relatively low level in Vlaardingen (a high level in Ommoord). If the former mean score-difference in a pair was larger than the latter it was said that this pair acted in a positive way. If, however the latter

mean score-difference was larger, this pair was said to have acted in a negative way.

Now in each CNSLD category (grade 0, 1, and 2+3) for each smoking category separately (smokers, non-smokers, and ex-smokers) the number of "positive" and "negative" pairs was counted. By means of the sign test the null-hypothesis of no "effect" of air pollution (i.e. equal probabilities for a random pair to act in a positive or in a negative way) was tested against a positive "effect" (i.e. a larger probability to act in a positive way).

Combining categories.

Because it was found desirable to make one statement for each CNSLD category concerning the influence of an air pollutant on the respiratory symptoms or on the irritation of the eyes, the smoking categories within a CNSLD category were combined (numbers in different smoking categories were added) and a sign test was performed for each of the three CNSLD categories separately. Analogously, the CNSLD categories within one smoking category were combined (by adding the numbers in the different CNSLD categories) and a sign test was performed for each of the three smoking categories separately.

Finally all nine CNSLD — smoking cells were combined (by adding the corresponding numbers) and the influence of an air pollutant on a particular respiratory symptom or on the irritation of the eyes was tested again by means of the sign test.

Testing differences in "effect" between categories.

If an association was found between an air pollution variable and a particular symptom when all nine CNSLD — smoking cells were combined, it was tested whether the "effect" differed *between* CNSLD categories or *between* smoking categories.

Let us denote by p_{hi} the probability of a "positive effect" for a random pair in CNSLD category i ($i=0,1,2$, the latter including category 3) and smoking category h ($h=1$ means smokers, $h=2$: non-smokers, $h=3$: ex-smokers).

The hypothesis of no difference between the CNSLD categories:

$$p_{ho} = p_{h1} = p_{h2} \quad (h=1,2,3)$$

was tested against the alternative:

$$p_{ho} \leq p_{h1} \leq p_{h2} \quad (h=1,2,3)$$

with at least one inequality strict, according to Schaafsma (1966), Chapter 5.6, formulae (5.20), (5.8), and (5.6).

The hypothesis of no difference between the smokers and non-smokers:

$$p_{1i} = p_{2i} \quad (i=0,1,2)$$

was tested against the alternative:

$$p_{1i} \leq p_{2i} \quad (i=0,1,2) \text{ or } p_{1i} \geq p_{2i} \quad (i=0,1,2)$$

with at least one inequality strict, by using a two-sided version of the test described in Schaafsma (1966), Chapter 5.6, formulae (5.20), (5.8) and (5.6).

If a significant "effect" was found only in smoking category h (in which the CNSLD categories were combined), it was tested whether the "effect" differed *between* the CNSLD categories within this smoking category. The hypothesis and the alternative are similar to the above case, but restricted to smoking category h . The performance of the test is also similar.

If a significant "effect" was found only in CNSLD category i (in which the smoking categories were combined), it was tested whether the "effect" differed *between* the smokers and non-smokers. The numbers of "positive" and "negative" pairs in these two smoking categories were arranged in a 2×2 contingency table and testing was performed by means of Fisher's exact test.

3.4. TESTING THE INFLUENCE OF AIR POLLUTION ON THE PEAK FLOW.

The peak flow measurements were carried out once a week, on the same day in both members of a pair. No measurements were carried out on Saturdays and Sundays.

To compare the fluctuations in the peak flow values of one person with those of another person, it was thought best to use the relative deviation of a peak flow value from a person's average and not the absolute values. Therefore, for each person

for each day the relative deviation (in the following called "the score") from the person's average was calculated. Having matched pairs, only score-differences were considered. By the score-difference is meant: the score of the Vlaardingen member minus the score of the Ommoord member of a pair on a particular day.

Comparing "effects" on several days with high levels of air pollution in Vlaardingen with "effects" on several days with relatively low levels of air pollution in Vlaardingen could lead to the comparison of score-differences between days, in which partly the same pairs and partly different pairs participated. Because a statistical analysis would then become extremely difficult, if not impossible, it was decided to select only two days, one with a very high level of air pollution in Vlaardingen, and another one with a relatively low level of air pollution in Vlaardingen (see section 3.2., Category C).

Now, two cases have to be distinguished: the one case in which both selected days are on the same day of the week, and the other case in which both days are on different days of the week. In the first case the same pairs are involved on both days, whereas in the second case different pairs are involved.

Case I: both selected days are on the same day of the week. For each pair participating on both days the score-difference on the polluted day in Vlaardingen minus the score-difference on the relatively low polluted day in Vlaardingen was calculated. It is assumed that with each participating pair a random variable is associated of which this value is an outcome. The random variables are considered mutually independent and normally distributed, with equal but unknown variance. Let us denote the expected value by μ_{hi} if the pair belongs to CNSLD category i ($i=0,1,2$, the latter including category 3) and smoking category h ($h=1,2,3$, $h=1$ means smokers, $h=2$: non-smokers, $h=3$: ex-smokers). In each CNSLD and smoking category the hypothesis of no effect:

$$\mu_{hi} = 0$$

was tested against the alternative of a negative effect on the peak flow:

$$\mu_{hi} < 0$$

by means of Student's one-sample t test.

Case II: the selected days are on different days of the week. The score-difference of a pair on one of the selected days is considered as the outcome of a normally distributed random variable. The random variables associated with different pairs are considered mutually independent with a variance which is equal for all pairs and for both days. The expected value is denoted by $\mu_{hi}^{(1)}$ if the score-difference is considered of a pair belonging to CNSLD category i and smoking category h (i and h as in case I) on the polluted day in Vlaardingen, and by $\mu_{hi}^{(2)}$ on the relatively low polluted day in Vlaardingen. In each CNSLD and smoking category the hypothesis of no effect:

$$\mu_{hi}^{(1)} = \mu_{hi}^{(2)}$$

is tested against the alternative of a negative effect:

$$\mu_{hi}^{(1)} < \mu_{hi}^{(2)}$$

by means of Student's two-sample t test.

Combining categories.

Case I.

It was found desirable to combine the different smoking categories within a CNSLD category. In each CNSLD category i the hypothesis of no effect:

$$\mu_{hi} = 0 \quad (h=1,2,3)$$

was tested against the alternative:

$$\mu_{hi} \leq 0 \quad (h=1,2,3)$$

with at least one inequality strict. The test was performed by means of the theory of Schaafsma (1966), Chapter 4.2, theorem 2. Analogously, the CNSLD categories within a smoking category were combined. In each smoking category h the hypothesis of no effect:

$$\mu_{hi} = 0 \quad (i=0,1,2)$$

was tested against the alternative:

$$\mu_{hi} \leq 0 \quad (i=0,1,2)$$

with at least one inequality strict. The test was performed by means of the above mentioned theory of Schaafsma.

Finally, all nine CNSLD - smoking cells were combined and the hypothesis:

$$\mu_{hi} = 0 \quad (i=0,1,2; h=1,2,3)$$

was tested against the alternative:

$$\mu_{hi} \leq 0 \quad (i=0,1,2; h=1,2,3)$$

with at least one inequality strict, by means of the above mentioned theory of Schaafsma.

Case II.

The combination of different smoking categories within CNSLD category i , now leads to the hypothesis:

$$\mu_{hi}^{(1)} = \mu_{hi}^{(2)} \quad (h=1,2,3)$$

and the alternative:

$$\mu_{hi}^{(1)} \leq \mu_{hi}^{(2)} \quad (h=1,2,3)$$

with at least one inequality strict. Here the theory of Schaafsma (1966), Chapter 5.2, theorem 2, was applied.

Combining different CNSLD categories within a particular smoking category h leads to the hypothesis:

$$\mu_{hi}^{(1)} = \mu_{hi}^{(2)} \quad (i=0,1,2)$$

and the alternative:

$$\mu_{hi}^{(1)} \leq \mu_{hi}^{(2)} \quad (i=0,1,2)$$

with at least one inequality strict. Again the theory of Schaafsma (1966), Chapter 5.2, theorem 2, was applied.

Finally, all nine CNSLD - smoking cells were combined and the hypothesis:

$$\mu_{hi}^{(1)} = \mu_{hi}^{(2)} \quad (i=0,1,2; h=1,2,3)$$

was tested against the alternative:

$$\mu_{hi}^{(1)} \leq \mu_{hi}^{(2)} \quad (i=0,1,2; h=1,2,3)$$

with at least one inequality strict, by applying the same theory of Schaafsma.

Testing differences in "effect" between categories.

If a negative "effect" was found significant in the combined test on a smoking category h , or in the combined test on all nine cells, it was tested whether the "effect" increased with degree of CNSLD.

Case I: in this case the hypothesis of no difference is formulated as:

$$\mu_{h0} = \mu_{h1} = \mu_{h2} \quad (\text{only for smoking category } h \text{ or for } h=1,2,3 \text{ respectively})$$

and the alternative of an increasing effect:

$$\mu_{h2} \leq \mu_{h1} \leq \mu_{h0} \quad (\text{only for smoking category } h \text{ or for } h=1,2,3 \text{ respectively})$$

with at least one inequality strict. A test for this situation is again given by Schaafsma (1966) Chapter 5.2, theorem 2.

Case II: here the hypothesis of no difference is formulated as:

$$\mu_{h0}^{(1)} = \mu_{h1}^{(1)} = \mu_{h2}^{(1)}, \mu_{h0}^{(2)} = \mu_{h1}^{(2)} = \mu_{h2}^{(2)} \quad (\text{only for smoking category } h \text{ or for } h=1,2,3 \text{ respectively})$$

and the alternative of an increasing effect on both days:

$$\mu_{h2}^{(1)} \leq \mu_{h1}^{(1)} \leq \mu_{h0}^{(1)}, \mu_{h0}^{(2)} \leq \mu_{h1}^{(2)} \leq \mu_{h2}^{(2)} \quad (\text{only for smoking category } h \text{ or for } h=1,2,3 \text{ respectively})$$

with at least one inequality strict. This test was also performed according to Schaafsma (1966) Chapter 5.2, theorem 2.

If a negative "effect" was found significant in the combined test on a CNSLD category i , or in the combined test on all nine

cells, it was tested whether the "effect" differed between smokers and non-smokers.

Case I: in this case the hypothesis of no difference is formulated as:

$$\mu_{1i} = \mu_{2i} \quad (\text{only for CNSLD category } i \\ \text{or for } i=0,1,2 \text{ respectively})$$

and the alternative as:

$$\mu_{1i} \leq \mu_{2i} \text{ or } \mu_{1i} \geq \mu_{2i} \quad (\text{only for CNSLD cate-} \\ \text{gory } i \text{ or for } i=0,1,2 \\ \text{respectively})$$

with at least one inequality strict. For the performance of this test the two-sided version of the test described in Schaafsma (1966), Chapter 5.2, theorem 2, was used.

Case II: here the hypothesis of no difference in "effect" between smokers and non-smokers is formulated as:

$$\mu_{1i}^{(1)} = \mu_{2i}^{(1)}, \mu_{1i}^{(2)} = \mu_{2i}^{(2)} \quad (\text{only for CNSLD} \\ \text{category } i \text{ or} \\ \text{for } i=0,1,2 \\ \text{respectively})$$

and the alternative of a certain difference as:

$$\mu_{1i}^{(1)} \leq \mu_{2i}^{(1)}, \mu_{2i}^{(2)} \leq \mu_{1i}^{(2)} \text{ or } \mu_{2i}^{(1)} \leq \mu_{1i}^{(1)}, \mu_{1i}^{(2)} \leq \mu_{2i}^{(2)} \\ (\text{only for CNSLD} \\ \text{category } i \text{ or} \\ \text{for } i=0,1,2 \\ \text{respectively})$$

with at least one inequality strict. For this situation the two-sided version of the test described in Schaafsma (1966), Chapter 5.2, theorem 2, was also used.

Special thanks are due to Mr. S. Knijpstra, statistician, TNO Research Unit for Epidemiology of CNSLD.

Note: For details on the statistical tests used the reader is referred to:

P. Armitage, Statistical Methods in Medical Research, Blackwell Scientific Publications.

H. de Jonge, Inleiding tot de Medische Statistiek, deel I en II, Verhandeling XLI en XLVIII van het Nederlands Instituut voor Praeventieve Geneeskunde, Leiden.

CHAPTER VI

RESULTS

1. THE POPULATION.

The actual survey started in the second week of January 1973 when the women were visited at home for instructions and the diaries were handed out, and consequently the number of women participating rose steeply in the first few weeks. The women were asked not to fill in their diaries when going on holidays, so in the summer months (from the end of June until the middle of August) there was a temporarily drop in the participation. Moreover, no home visits were made in July because of holidays by the staff. The survey ended in the last weeks of December 1973.

During the year of investigation 105 individuals were lost, which is 13,3% of the initial total population of 792 individuals. Of the 105 individuals 53 moved to another area of residence and the other 52 withdrew from participation for various reasons (no interest, illness, et cetera). As can be seen from table 6.1., there are only slight and not consistent differences in the number of women lost between Vlaardingen and Ommoord within each CNSLD category. There is a slight excess of women lost in the first quarter, mainly because of retracting the initial promise to participate. The 105 individuals included 12 pairs, so at the end of the year not 105 pairs were lost, but only 93 pairs. Table 6.2. shows that there are only slight differences in the percentages of pairs under investigation between the different CNSLD categories at the end of each quarter, adding grade 3 because of the small numbers to grade 2. These differ-

Table 6.1. Number of individuals lost during each quarter of the year according to degree of CNSLD and area of residence, and in addition the number of pairs lost as a consequence.

DEGREE		QUARTER OF THE YEAR								TOTAL NUMBER			
OF		first		second		third		fourth		Total		LOST	
CNSLD		Vl.	Om.	Vl.	Om.	Vl.	Om.	Vl.	Om.	Vl.	Om.	indiv.	pairs
grade 0		10	8	4	1	6	8	4	4	24	21	45	39
grade 1		7	6	1	1	4	6	2	6	14	19	33	30
grade 2		7	3	1	2	1	4	3	3	12	12	24	21
grade 3		0	1	1	0	0	1	0	0	1	2	3	3
Total		24	18	7	4	11	19	9	13	51	54	105	93
TOTAL	indiv.	42		11		30		22		105			
NUMBER	pairs	40		11		25		17		93			
LOST													

Table 6.2. Number of pairs under investigation at the end of each quarter of the year according to degree of CNSLD.

DEGREE		QUARTER OF THE YEAR							
OF CNSLD	N _t	first		second		third		fourth	
		n	%	n	%	n	%	n	%
grade 0	150	133	88,6	128	85,3	116	77,3	111	74,0
grade 1	128	116	90,6	114	89,1	106	82,8	98	76,6
grade 2	112	102	91,1	99	88,4	95	84,8	91	81,2
grade 3	6	5	83,3	4	66,7	3	50,0	3	50,0
Total	396	356	89,9	345	87,1	320	80,0	303	76,5

ences proved not to be significant with a chi-square test on 2x3 contingency tables.

As only those data could be analyzed that were obtained in both members of a pair on the same days, it was very fortunate that the women cooperated extremely well.

2. DIARY DATA AND PEAK FLOW MEASUREMENTS.

2.1. RESPIRATORY SYMPTOMS.

The figures C 1 to 4 (Appendix C) show the daily mean score-differences between Vlaardingen and Ommoord for the respiratory symptoms according to degree of CNSLD. In the group CNSLD grade 0 the daily mean score-differences fluctuate only slightly and are generally about zero. The greatest fluctuations of the daily mean score-differences can be seen in the group CNSLD grade 2+3. In this group there is on the whole a positive daily mean score-difference for the symptoms dyspnoea and wheezing, and on the contrary a negative one for the symptoms cough and phlegm. The group CNSLD grade 1 is intermediate as regards the extent of the fluctuations and the position of the curve representing the daily mean score-differences, except for the symptom cough. For this symptom the position of the curve is above the other two grades, and furthermore the daily mean score-difference is nearly always positive.

Comparing the graphs of the respiratory symptoms to the graphs of the air pollutants (figures D 1 to 10), it can be seen that only for the symptoms dyspnoea and wheezing in the group CNSLD grade 2+3 there is a trend that some of the periods of great daily mean score-differences correspond with periods of high levels of some air pollutants.

2.2. IRRITATION OF THE EYES.

The daily mean score-differences fluctuate to about the same extent in the three CNSLD groups, and are on the whole slightly positive (see figure C 5). In general, no parallelism can be seen between the fluctuations of the daily mean score-differ-

ences in the CNSLD groups, except in a few periods. These periods tend to correspond with periods of high pollution levels of ozone in Vlaardingen (figures D 7 and 8).

2.3. PEAK FLOW MEASUREMENTS.

From figure C 6, presenting the daily mean of the differences in "percentage difference from the mean" between Vlaardingen and Ommoord according to degree of CNSLD, no distinctive patterns can be traced.

3. SPUTUM COLLECTION.

Table 6.3. shows the number of times sputum was collected in Vlaardingen and Ommoord in relation to the answer on the production of phlegm ticked in the diary on the day of the home visit, having added together all the available data of all individuals.

Table 6.3. Sputum collection in relation to the answer on the production of phlegm.

ANSWER TICKED IN THE DIARY	SPUTUM COLLECTED			
	VLAARDINGEN		OMMOORD	
	YES	NO	YES	NO
YES	254	1431	355	1665
NO	15	12939	27	12394

In general, the answer and the collection correspond well. Only a very few times sputum was handed in while the answer on phlegm in the diary was NO. However, relatively frequently no sputum was handed in while the answer on phlegm in the diary was positive. A reasonable explanation for this disagreement is that only sputum brought up in the first hour after getting up on the day of the home visit had to be handed in.

It appeared that in Vlaardingen 56 women, and in Ommoord 57 women, contributed to the number of times sputum was handed in.

Furthermore, of these women 24 in Vlaardingen and 40 in Ommoord ever handed in mucopurulent or purulent sputum, while in total during the year of investigation 51 times in Vlaardingen and 172 times in Ommoord (muco)purulent sputum was handed in. This points to the possibility that bacterial respiratory infections occurred more frequently in Ommoord than in Vlaardingen. However, because of the relatively small numbers involved, it is not likely that intercurrent bacterial respiratory infections would have been a disturbing factor in this study.

4. AIR POLLUTION DATA.

From the graphs in the figures D 1 to 10 (Appendix D) it can be seen that the air pollution levels in Vlaardingen are generally above those in Ommoord with the exception of the levels of the aldehydes. In general, the fluctuations of the air pollution levels in Vlaardingen and Ommoord run parallel. During days of very high pollution the levels in Vlaardingen are well above those in Ommoord, particularly those of SO_2 and NO_2 . However, in general the differences in air pollution levels between Vlaardingen and Ommoord are less than was expected before the start of the study.

As an explanation one can propose that the site of Ommoord - northeast of the petrochemical complex along the "Rotterdamse Waterweg" - and the winds prevailing west and south can give rise to a substantial air pollution level in Ommoord, particularly of aldehydes which are formed in the process of photochemical oxidation taking place in the atmosphere some time after the primary pollutants have been emitted.

By means of applying a statistical method of analyzing the data obtained on those days that the air pollution levels in Vlaardingen and Ommoord were contrastive, it was tried to provide the best opportunity to detect differences with respect to the respiratory parameters.

TABLE 6.4. The percentiles of the individual air pollutants in Vlaardingen (Vl.) and Ommoord (Om.) expressed in $\mu\text{g}/\text{m}^3$.

AIR POLLUTANT	AREA	10 PERC.	20 PERC.	30 PERC.	40 PERC.	50 PERC.	60 PERC.	70 PERC.	80 PERC.	90 PERC.	95 PERC.	99 PERC.
Sulphur dioxide	Vl.	22	35	44	55	68	83	103	126	164	187	327
24-hour average	Om.	10	19	24	30	40	48	65	79	100	127	178
Standard smoke	Vl.	5	6	8	10	13	17	23	28	38	50	75
24-hour average	Om.	4	5	7	10	12	16	20	24	38	52	70
Nitrogen monoxide	Vl.	6	10	14	17	21	27	37	51	65	79	163
daily average	Om.	4	6	7	9	11	13	16	23	39	50	86
Nitrogen monoxide	Vl.	11	18	26	40	49	65	86	112	168	265	610
daily maximum	Om.	8	11	16	22	26	33	45	64	104	142	248
Nitrogen dioxide	Vl.	19	24	28	33	37	42	49	58	70	87	100
daily average	Om.	17	21	25	28	31	34	37	43	51	58	76
Nitrogen dioxide	Vl.	31	42	52	58	67	76	83	93	119	137	180
daily maximum	Om.	31	38	44	50	56	60	64	72	83	103	150
Ozone	Vl.	16	24	29	34	38	43	48	55	70	90	117
daily average	Om. ¹⁾	20	20	20	20	25	25	30	38	50	55	65
Ozone	Vl.	25	36	47	55	64	69	75	95	135	160	230
daily maximum	Om. ¹⁾	25	25	25	25	35	35	45	55	65	85	95
Aldehydes	Vl.	16	24	29	33	38	46	54	64	75	89	139
24-hour average	Om. ¹⁾	23	26	34	45	56	72	84	99	134	151	176
Aldehydes	Vl.	23	36	45	57	67	83	95	113	144	174	320
8-hour average	Om. ¹⁾	25	31	38	49	64	83	126	171	246	318	367

¹⁾ percentiles in Ommoord computed only from day 213 (see Chapter IV, section 6).

5. METEOROLOGICAL DATA.

The graphs in the figures E 1 to 4 (Appendix E) show that the temperature and the relative humidity in Vlaardingen and Ommoord correspond so well that the assumption of similar meteorological conditions in both areas was warranted.

So it is also justifiable to assume similar wind characteristics in both areas as well and consequently, although wind has a great influence on the air pollution levels, they could possibly not have affected the actual results of this comparative study.

6. THE SELECTED DAYS FOR THE ANALYSIS.

Table 6.4. shows the percentiles computed for each pollutant in Vlaardingen and Ommoord by means of which days were selected for the analysis.

The days were numbered according to the order of sequence in the year, starting from the first of January (day 1.). In the tables 6.5., 6.6., and 6.7. the numbers of the selected days according to the criteria as set in Chapter V, section 3.2., are shown respectively for category A (days with high pollution levels), category B (days with peak pollution levels), and category C (days from the categories A and B for the analysis of the peak flow data).

In category A a few alternative days had to be selected, as it was not always possible to fulfil the criteria. In category A-1 the numbers 294 and 329 indicate days when the air pollution levels in Ommoord for standard smoke and aldehydes 8-hour average were the lowest recorded during the year of investigation. In category A-2 the numbers 320 and 27 indicate days when the air pollution levels in Vlaardingen for nitrogen monoxide daily average and ozone daily maximum were the lowest recorded during the year of investigation.

In category B-1 no days could be selected for nitrogen monoxide daily average and aldehydes 24-hour average, and in category B-2 for nitrogen monoxide daily average, as the set criteria could

Table 6.5. The numbers of the selected days in category A.

NUMBERS OF THE DAYS		
AIR POLLUTANT	CATEGORY A-1	CATEGORY A-2
Sulphur dioxide		
24-hour average	217 and 218	43, 54, 60, 61, and 79
Standard smoke		
24-hour average	294 ¹⁾	84
Nitrogen monoxide		
daily average	165, 256, and 302	320 ²⁾
daily maximum	248, 302, and 323	61 and 82
Nitrogen dioxide		
daily average	107, 239, 278, and 279	64, 87, and 331
daily maximum	107, 182, 185, and 278	87 and 89
Ozone		
daily average	232, 236, and 239	254
daily maximum	236, 239, 247, 250, and 251	27 ²⁾
Aldehydes		
24-hour average	278 and 307	274
8-hour average	329 ¹⁾	224, 259, 260, 263, 274, and 275

¹⁾ Alternative day: the day of lowest concentration in Ommoord.

²⁾ Alternative day: the day of lowest concentration in Vlaardingen.

Table 6.6. The numbers of the selected days in category B.

AIR POLLUTANT	NUMBERS OF THE DAYS	
	CATEGORY B-1	CATEGORY B-2
Sulphur dioxide		
24-hour average	33, 34, 35, and 82	60 and 64
Standard smoke		
24-hour average	278 and 279	32, 33, and 84
Nitrogen monoxide		
daily average	no day	no day
daily maximum	297	82
Nitrogen dioxide		
daily average	107, 278, and 299	80
daily maximum	107, 250, 258, and 278	166 and 247
Ozone		
daily average	239 and 248	254
daily maximum	247 and 248	254
Aldehydes		
24-hour average	no day	227 and 274
8-hour average	248	226, 229, 260, and 263

Table 6.7. The numbers of the selected days in category C.

AIR POLLUTANT	NUMBERS OF THE DAYS	
	CATEGORY C-1	CATEGORY C-2
Sulphur dioxide		
24-hour average	218	253 ³⁾
Standard smoke		
24-hour average	278	130 ³⁾
Nitrogen monoxide		
daily average	302	320 ³⁾
daily maximum	297	320 ³⁾
Nitrogen dioxide		
daily average	278	331
daily maximum	107	247
Ozone		
daily average	239 ¹⁾	254
daily maximum	247 ¹⁾	254
Aldehydes		
24-hour average	278	274
8-hour average	295 ²⁾	226

¹⁾ Alternative day: the day of highest ozone concentration in Vlaardingen on which peak flow values were available

²⁾ Alternative day: the day of lowest aldehydes 8-hour average concentration in Ommoord, and on which peak flow values were available.

³⁾ Alternative day: the day of lowest concentration in Vlaardingen, and on which peak flow values were available.

not be fulfilled and in this category a suitable alternative approach did not emerge.

In category C a few alternative days were selected as mentioned in the footnotes in the table 6.7.

7. RESULTS OF THE ANALYSIS.

7.1. INTRODUCTION.

As described extensively in Chapter V, section 3., the testing on the influence of air pollution on the symptoms and the peak flow was carried out for separate categories as well as for combinations of categories. Consequently, four classes can be distinguished: "cell", "CNSLD category", "smoking category", and "total population". These classes are specified as follows:

"*Cell*": nine cells were composed by combining CNSLD and smoking categories in the following way:

CELL	CNSLD category	SMOKING category
1	grade 0	smoker
2	grade 0	non-smoker
3	grade 0	ex-smoker
4	grade 1	smoker
5	grade 1	non-smoker
6	grade 1	ex-smoker
7	grade 2+3	smoker
8	grade 2+3	non-smoker
9	grade 2+3	ex-smoker

"*CNSLD category*": the CNSLD categories grade 0, grade 1, and grade 2+3, in which categories the smoking categories are combined.

"*Smoking category*": the smoking categories of smokers, non-smokers, and ex-smokers, in which categories the CNSLD categories are combined.

"*Total population*": in which all CNSLD categories and all smoking categories are combined (all nine cells combined).

The last three classes can be considered as being combined cells. If in any of the cells or combinations of cells a significant result was found by testing the influence of a particular air pollutant on a particular symptom, this means that there is an association between high levels of that air pollutant and the prevalence—severity of that symptom in that cell or combination of cells. In the following such an association will be denoted simply as "association", "association between air pollutant and symptom", or "effect".

7.2. SYMPTOMS.

7.2.1. HIGH POLLUTION LEVELS.

The tables 6.8, 6.9, and 6.10. show the significant associations found by testing the influence of air pollutants on the symptoms in the four classes, using the data of the selected days in category A with a time lag respectively of 0 day, 1 day, and 2 days.

To illustrate the results an example will be given from table 6.8. with respect to standard smoke. An association is found between this pollutant and the symptom irritation of the eyes only. This association is found in the pairs who smoke, and in the total population in which case all pairs are involved. The testing on the separate cells and on the CNSLD categories did not yield any significant results.

Time lag of 0 day:

From table 6.8. it can be seen that associations are found between particularly nitrogen monoxide, ozone, and aldehydes and the symptoms. The associations within a CNSLD category are found with regard to the respiratory symptoms in grade 1 and grade 2+3 and with regard to irritation of the eyes in grade 0 and grade 1. The associations with this latter symptom occur also always in the total population. The associations between aldehydes and the symptoms are seen particularly in the category of the non-smokers.

Time lag of 1 day:

Table 6.9. shows that associations are found between especially nitrogen monoxide and ozone, and the symptoms, but also standard smoke, nitrogen dioxide, and aldehydes show some "effect". The associations within the CNSLD categories are again found in grade 1 and grade 2+3, while with respect to the smoking categories the associations are mainly seen in the categories of non-smokers and ex-smokers. The associations between air pollutants and irritation of the eyes are somewhat less pronounced than with a time lag of 0 day.

Time lag of 2 days:

The associations between air pollutants and the symptoms when applying a time lag of 2 days (table 6.10.) correspond in general lines with the associations found when applying a time lag of 1 day. However, there seems to be a slight change in the manifestation of the "effects", cough becoming more prevalent and irritation of the eyes less.

7.2.2. PEAK POLLUTION LEVELS.

Table 6.11. shows the significant associations found by testing the influence of air pollutants on the symptoms in the four classes according to time lag, using the data of the selected days in category B.

From this table it can be seen that specially ozone is involved in the association between the air pollutants and the symptoms. With a time lag of 0 day an association is found with irritation of the eyes, and with a time lag of 1 day and 2 days associations with the respiratory symptoms are more manifest, specially with cough and phlegm.

It appears that within the CNSLD categories the associations with the respiratory symptoms are rather frequently found in CNSLD grade 2+3.

7.3. PEAK FLOW.

The significant associations found between the air pollutants and the peak flow are presented in table 6.12.

Table 6.8. The associations found between air pollutants and symptoms for the selected days in Category A, with a time lag of 0 day.¹⁾

AIR POLLUTANT	SYMPTOM	CELL	CNSLD CATEGORY (smoking categories combined)	SMOKING CATEGORY (CNSLD categories combined)	TOTAL POPULATION (CNSLD and smoking categories combined)
Standard smoke	irritation of the eyes	-	-	smokers	+
Nitrogen monoxide					
daily average	phlegm	-	grade 1 ^x , and 2+3	smokers	+ ^{xxx}
daily maximum	phlegm	-	-	-	+
	dyspnoea	-	grade 1	-	- ^{xx}
	irritation of the eyes	2	grade 0 ^x	-	+ ^{xx}
Ozone					
daily maximum	cough	7 ^{xx}	grade 2+3 ^x	-	-
	phlegm	-	grade 2+3	-	-
	dyspnoea	7	grade 1	smokers	+ ^{xx}
	irritation of the eyes	2	grade 0, and 1 ^x	ex-smokers ^x	+ ^{xx}
Aldehydes					
24-hour average	phlegm	5 ^{xx} , 8	grade 1 ^x	non-smokers ^{xxx}	+ ^{xx} 2)
	dyspnoea	-	-	non-smokers	-
	wheezing	-	-	non-smokers	-
	irritation of the eyes	-	-	non-smokers ^{xx}	+ ^{xx}

1) Significant at the 5 per cent level, except x $P < 0.025$, xx $P < 0.010$, xxx $P < 0.005$.

2) Significant difference in "effect" between the smokers and non-smokers ($P < 0.05$).

Table 6.9. The associations found between air pollutants and symptoms for the selected days in Category A, *with a time lag of 1 day.*¹⁾

AIR POLLUTANT	SYMPTOM	CELL	CNSLD CATEGORY (smoking categories combined)	SMOKING CATEGORY (CNSLD categories combined)	TOTAL POPULATION (CNSLD and smoking categories combined)
Standard smoke	dyspnoea	5	-	non-smokers	-
Nitrogen monoxide					
daily average	phlegm	7 ^x	grade 1 ^x , and 2+3	-	+ xxx
daily maximum	dyspnoea	-	grade 1 ^x	ex-smokers ^x	+ xx
	wheezing	-	grade 2+3	ex-smokers	+
	irritation of the eyes	-	-	smokers	+ xx
Nitrogen dioxide					
daily maximum	phlegm	-	-	non-smokers	-
Ozone					
daily maximum	cough	7	grade 2+3 ^{xx}	smokers	- 2)
	phlegm	6	grade 2+3 ^x	ex-smokers ^x	+
	dyspnoea	-	-	ex-smokers	-
	irritation of the eyes	2 ^x	grade 0 ^{xxx}	non-smokers	+ xxx
Aldehydes					
24-hour average	phlegm	5, 8	-	non-smokers ^{xxx}	+ x 3)
	irritation of the eyes	-	-	-	+

1) Significant at the 5 per cent level, except x $P < 0.025$, xx $P < 0.010$, xxx $P < 0.005$.

2) Significant difference in "effect" between the CNSLD categories ($P < 0.025$).

3) Significant difference in "effect" between the smokers and non-smokers ($P < 0.025$).

Table 6.10. The associations found between air pollutants and symptoms for the selected days in Category A, with a time lag of 2 days.¹⁾

AIR POLLUTANT	SYMPTOM	CELL	CNSLD CATEGORY (smoking categories combined)	SMOKING CATEGORY (CNSLD categories combined)	TOTAL POPULATION (CNSLD and smoking categories combined)
Standard smoke	cough	2	-	non-smokers ^{xxx}	-
	dyspnoea	-	-	non-smokers	-
Nitrogen monoxide daily average	cough	-	grade 1	smokers ^x	+ ^x
	phlegm	-	grade 1, and 2+3	smokers and non-smokers	+ ^{xx}
daily maximum	dyspnoea	5	-	non-smokers ^{xx}	-
	wheezing	-	-	ex-smokers	+ ^x
	irritation of the eyes	7 ^x	-	smokers	+ ^x
Nitrogen dioxide daily maximum	phlegm	-	grade 2+3	-	-
Ozone daily maximum	cough	7 ^x	grade 2+3 ^{xxx}	smokers ^x	+ ^{xxx}
	phlegm	-	grade 2+3 ^{xxx}	ex-smokers	-
	irritation of the eyes	2 ^x	grade 0 ^{xx}	-	+
Aldehydes 24-hour average	dyspnoea	2	-	non-smokers	-

¹⁾ Significant at 5 per cent level, except x P < 0.025, xx P < 0.010, xxx P < 0.005.

Table 6.11. The associations found between air pollutants and symptoms for the selected days in Category B.¹⁾

AIR POLLUTANT	SYMPTOM	CELL	CNSLD CATEGORY (smoking categories combined)	SMOKING CATEGORY (CNSLD categories combined)	TOTAL POPULATION (CNSLD and smoking categories combined)
<i>Time lag of 0 day</i>					
Nitrogen monoxide daily maximum	irritation of the eyes	7	-	-	-
Ozone daily average	irritation of the eyes	2 ^{xx}	grade 0 ^x	non-smokers ^{xx}	+ ^{xxx}
daily maximum	irritation of the eyes	-	-	non-smokers	+
Aldehydes 8-hour average	cough	-	-	-	+ ^x
	irritation of the eyes	-	grade 1 ^{xxx} , and 2+3	smokers, non-smokers ^x , and ex-smokers ^x	+ ^{xxx}
<i>Time lag of 1 day</i>					
Nitrogen monoxide daily maximum	cough	1	-	-	-
	dyspnoea	5	grade 1 ^x	non-smokers	-
	irritation of the eyes	-	-	smokers ^x	-
Nitrogen dioxide daily maximum	cough	6	-	-	-

Table 6.11. (continued)

Ozone						
daily average	cough	7 ^x	grade 2+3	-	-	-
	irritation of the eyes	-	-	non-smokers ^x	-	+ ^x
daily maximum	cough	-	grade 2+3	-	-	-
	dyspnoea	7	grade 2+3	smokers ^x	-	+ ^{xxx}
	irritation of the eyes	2	grade 0 ^x , 1 ^x , and 2+3	smokers ^x , non-smokers	xxx	+ ^{xxx}
<i>Time lag of 2 days</i>						
Standard smoke	phlegm	5	-	-	-	-
	dyspnoea	-	grade 1	-	-	-
Nitrogen monoxide						
daily maximum	cough	-	grade 1	-	-	-
	phlegm	-	-	ex-smokers	-	-
Nitrogen dioxide						
daily average	phlegm	5	-	-	-	-
Ozone						
daily average	cough	7	grade 2+3	-	-	-
	irritation of the eyes	-	-	non-smokers	-	-
daily maximum	cough	-	grade 2+3 ^x	-	-	-
	phlegm	-	grade 2+3	-	-	-
	dyspnoea	-	-	-	-	+ ^{xx}
Aldehydes						
8-hour average	phlegm	8 ^{xxx}	grade 2+3 ^{xxx}	non-smokers ^x	-	+ 2)
	irritation of the eyes	-	-	non-smokers	-	-

1) Significant at 5 per cent level, except x P < 0.025, xx P < 0.010, xxx P < 0.005.

2) Significant difference in "effect" between the CNSLD categories (P < 0.005), and between the smokers and non-smokers (P < 0.010).

Table 6.12. The associations found between air pollutants and the peak flow for the selected days in Category C.¹⁾

AIR POLLUTANT	CELL	CNSLD CATEGORY (smoking categories combined)	SMOKING CATEGORY (CNSLD categories combined)	TOTAL POPULATION (CNSLD and smoking categories combined)
<i>Time lag of 0 day</i>				
Sulphur dioxide	7	-	-	-
Standard smoke	6, 8 ^{xxx}	-	-	+
Nitrogen monoxide daily maximum	-	-	smokers	-
Ozone daily average	4	-	-	-
Aldehydes 8-hour average	6 ^x	-	-	-
<i>Time lag of 1 day</i>				
-	-	-	-	-
<i>Time lag of 2 days</i>				
Sulphur dioxide	2 ^{xx}	-	-	-
Ozone daily average	8 ^{xx}	-	-	-
daily maximum	-	grade 0	-	-
Aldehydes 8-hour average	4 ^{xxx}	grade 1 ^{xx}	smokers	-

1) Significant at 5 per cent level, except x P < 0.025, xx P < 0.010, xxx P < 0.005.

The few associations found when applying a time lag of 0 day and 2 days do not show any distinct pattern, while no association at all is found with a time lag of 1 day.

7.4. SUMMARY.

Associations were mainly found between the air pollutants nitrogen monoxide, ozone, and aldehydes on the one hand, and both respiratory symptoms and irritation of the eyes on the other hand.

The respiratory symptoms cough, phlegm, and dyspnoea were frequently involved in the associations found, and wheezing only very occasionally.

There is an indication of an immediate "effect" (time lag of 0 day) especially on irritation of the eyes, and of a more delayed effect (time lag 1 day and 2 days) on the respiratory symptoms, particularly on cough.

The associations found within the CNSLD categories are seen particularly in the subjects with moderate to severe degree of CNSLD (grade 2+3).

The associations between aldehydes and the symptoms are seen above all in the non-smokers. Furthermore, there is a slight indication that non-smokers and ex-smokers are more affected than smokers by high levels of air pollution with a time lag of 1 day and 2 days.

Hardly any associations between air pollutants and the peak flow are found.

It is noticeable that sulphur dioxide did not yield any associations, and standard smoke and nitrogen dioxide only a very few.

CHAPTER VII

DISCUSSION

Study design.

This epidemiological investigation was set up to find out whether there existed an association between high levels of air pollution of short duration in the Rijnmond area and an excess respiratory morbidity.

Special features of the study were, that only a female population was studied, that a control population was individually matched to the study population with respect to age, degree of CNSLD, and smoking habit, and that attention was paid to whether persons with CNSLD differed "in reaction" from persons without CNSLD. Furthermore, weekly home visits were carried out to obtain optimum cooperation of the women, and gave the opportunity to perform a simple lung function test at the women's homes. A female population was studied because women are less exposed to the occupational hazards of pollution than men, are often less severe smokers than men, and can usually be visited at home easily.

The method of using matched pairs in an attempt to eliminate certain confounding factors proved to be successful as only relatively few people were lost during the year of investigation. In this respect the personal contacts during the weekly home visits were extremely useful and essential in stimulating the subjects to carry on participating.

For obtaining data on the symptoms a diary technique was used as was successfully applied by Lawther et al. (1970) previously. However, the questions in the diary used in this study were more extensive and a total of five questions had to be answered each

day. Because of this, it was felt essential to keep the filling in of the diary as simple as possible. So a diary, specially designed for this study, was printed in which the women had simply to tick the respective spaces. The home visits played a significant part in the achievement of the proper filling in of the diaries when checked once a week.

During the home visits a lung function test was carried out initially only with the Monaghan spirometer, later also with the Wright Peak Flow meter. In this study it was felt that there is a definite need for well established simple lung function instruments reliable and suitable in field surveys, and if possible with automatic recording. Such instruments are now being developed (Derrett and Brown, 1975).

The lung function measurements were carried out once a week in all subjects, but likely more useful data would have been obtained by at least one daily measurement and ideally by more frequent daily measurements, even if only in a subsample of the population. However, this could organizationally not be achieved.

For the purpose of this study criteria were designed to be able to allocate the subjects to different grades of CNSLD, from no CNSLD (grade 0) to severe degree of CNSLD (grade 3). Although the criteria were identical to subdivide the population in Vlaardingen and Ommoord into the four grades of CNSLD, it is still possible that the members of a pair being matched on degree of CNSLD had different manifestations of CNSLD possibly leading to a different reaction pattern to air pollution. Moreover, - if the hypothesis is true that air pollution is one of the exogenous aetiological factors in the development of CNSLD - it might have been possible that, for example, a person with CNSLD grade 1 in Ommoord would have been classified as having CNSLD grade 2 if that person would have lived in Vlaardingen because of additional symptoms leading to a higher grading. But it is not likely that these factors would have influenced the results.

It is worth mentioning that both in Vlaardingen and Ommoord in the CNSLD categories grade 2 and 3 quite a considerable number

of non-smoking individuals are found (see Chapter IV, table 4.3.). This supports the hypothesis that smoking is only *one* of the major factors in the development of CNSLD.

It would have been preferable to have had a larger study population, because in this study it proved to be difficult to acquire a reasonably large number of women aged 18-42 years in the CNSLD categories grade 2, and especially grade 3. This was not beyond expectation (Van der Lende, 1969).

Later Van der Lende et al. (1975^C) found from a prevalence study on chronic non-specific lung disease carried out in Vlaardingen in 1972 in the *same* sample of women aged 18-42 years that 3.4% had a moderate degree of CNSLD and 1.4% a severe degree of CNSLD. In men aged 18-42 years 4.1% had a moderate degree of CNSLD and 2.5% a severe degree of CNSLD. Although the prevalence of CNSLD in subjects in the older age-groups is somewhat higher (Zuiderweg, 1962; Van der Lende et al., 1975^C) it was thought better to study people in a younger age-group because their airways have been less exposed to various exogenous stimuli during their lifetime.

Moreover, Lawther and Waller (personal communication) found that groups of about 1,000 people were needed to isolate environmental factors from the background "noise" of random illnesses. However, organizationally a limit was imposed on the extent of the study.

Data analysis.

Because matched pairs were used in the study, only those data could be analyzed that were available in *both* members of a pair. The data in the diary were given a score in an attempt to add weight to the answer of the respective question, which did not refer to the previous day but to the "as usual" situation. In this way, only differences in scores between the Vlaardingen and the Ommoord member of a pair could be taken into account in the analysis. For each symptom mean daily score-differences were computed to which both the height of the scores and the number of participating pairs on that day contributed. In this

study, it was felt that the use of a scoring system would be more adequate to reveal possible associations between high daily air pollution levels and symptoms, rather than the use of a no-yes answer system which would yield a mere daily prevalence of the symptoms, obscuring the severity or the change in severity of the symptoms.

As described in Chapter V, section 2.1., there is in general a positive mean score-difference between Vlaardingen and Ommoord in the group CNSLD grade 2+3 (moderate to severe degree of CNSLD) for the symptoms dyspnoea and wheezing, and a negative one for the symptoms cough and phlegm. This may mean a higher prevalence of the symptoms dyspnoea and wheezing in the Vlaardingen members in comparison to the Ommoord members with CNSLD grade 2+3, and accordingly a lower prevalence of cough and phlegm.

The former findings are in accordance with the findings by Van der Lende et al. (1973^a) who found a higher prevalence of the symptom dyspnoea in Vlaardingen in the age-group of 15-39 years as compared with a rural district. The data on the sputum collection in this study (see Chapter VI, section 3.) are in accordance with the latter findings.

In spite of the fact that Ommoord was in a way an ideal district to acquire a control population, it was unfortunate that the air pollution levels in Ommoord were higher than expected, limiting the analysis of the data to a relatively small number of days making the results possibly less conclusive. It was thought best to analyze the data of days with contrastive air pollution levels in Vlaardingen and Ommoord implicating that only days could be involved in the analysis on which air pollution data were available both in Vlaardingen and Ommoord. As a result, it happened that some highly polluted days and sometimes longer periods had to be left out for a particular pollutant in the analysis, because either no data were available or the data were unreliable as regards that pollutant.

In view of the possibility of ebbing and lagging of effects a time interval had to exist for each pollutant of at least three

days between the selected days of high pollution in Vlaardingen and the selected days of relatively low pollution in Vlaardingen. A longer time interval would have been preferable, but unfortunately days of high pollution levels in Vlaardingen and Ommoord were often very close together, as can be seen from the graphs in Appendix D. Therefore, a time lag of not more than two days was used in the analysis of the data. It occurred that selected days for one pollutant coincided with selected days for another pollutant making it difficult to isolate effects of the pollutants involved. Occasionally coincidence occurred within a set of selected days for a particular pollutant which might have increased the effects found at one or more of the time lags. However, all days that complied with the set criteria were selected hoping for a stronger evidence - if any - from the analysis rather than selecting only two contrastive polluted days. In this latter case "effects" might be present but not strong enough to yield a significant result in the testing procedure.

Results.

From the analysis of the data a few interesting findings have emerged.

It was found that mainly the photochemical pollutants, in particular nitrogen monoxide, ozone, and aldehydes, were related to the symptoms, which indicates that photochemical air pollution may play an important part in the Rijnmond area, as was recently also suggested by Biersteker (1975). In this respect it is noteworthy that of the nitrogen oxides nitrogen monoxide produced the most "effects" and nitrogen dioxide only a very few. This finding needs further investigation because nitrogen monoxide is a major product of fuel combustion processes at very high temperatures (especially from motor vehicles) and a major component of the smoke from cigarettes. The more so because the experimental studies on nitrogen oxides were mainly carried out with nitrogen dioxide because the concentration of nitrogen monoxide is very difficult to control as nitrogen monoxide at high concentrations is readily oxidized to nitrogen dioxide

(see Chapter I, section 5.2.).

In this study no associations at all were found between high levels of sulphur dioxide and the prevalence — severity of symptoms, possibly because the levels of sulphur dioxide have not been high enough during the year of investigation to produce any effects. In fact, this is not so surprising as the levels of sulphur dioxide and also of standard smoke have decreased considerably in the last decade (Biersteker, 1972), and were well below the minimum pollution leading to any significant response as was found to be about $500 \mu\text{g}/\text{m}^3$ of sulphur dioxide together with about $250 \mu\text{g}/\text{m}^3$ of smoke (24-hour averages) by Lawther et al. (1970). Another factor possibly is that in experimental studies on effects of sulphur dioxide in patients with CNSLD, effects were particularly seen in individuals with "asthma" (allergic patients) (Gökemeijer, 1976), whereas in the study population only a limited number of individuals with "allergy" can be assumed. This is based on the findings from an epidemiological study in 1969 in a random sample of the population in Vlaardingen that only 6.7% of the women of corresponding age as in the study population had both eosinophilia in the blood (more than $330 \text{ eosinophils}/\text{mm}^3$) and at least one skintest positive out of four (house dust, mixed pollen, mixed moulds, mixed epidermal products) (Wever-Hess and Van der Lende, 1971). In view of the findings by Biersteker (1972) and Lawther et al. (1970) it is conceivable that only a few associations were found between standard smoke and the symptoms as the levels of standard smoke proved to be relatively low in the Rijnmond area.

The respiratory symptoms cough, phlegm, and dyspnoea were frequently involved in the associations found, and wheezing only very occasionally. There is an indication that high levels of air pollution have a more immediate effect on irritation of the eyes, and a more delayed effect on the respiratory symptoms, in particular cough. This finding is in accordance with other observations indicating an immediate effect on irritation of the eyes and of a delayed effect on the symptom cough by in particular sulphur dioxide (e.g. McCarroll et al., 1967).

There is some difference between the results of the analysis of the data of the selected days with high pollution levels (category A) and peak pollution levels (category B).

The methods for the selection of the days are described in Chapter V, section 3.2. The days with peak pollution levels reveal fewer associations between air pollutants and symptoms, while fewer respiratory symptoms are involved in these associations (see the tables 6.8. to 6.11., p. 109 to p. 113). The criteria for selecting the days in category B were such that the peak pollution levels in Vlaardingen could go with also high pollution levels in Ommoord (and vice versa) which proved often to be the case, possibly obscuring associations between air pollutants and symptoms as a result of consequent small score-differences between the members of the pairs. As associations were still found between air pollutants and particularly the symptoms cough and irritation of the eyes it is suggested that these symptoms might be sensitive indicators in assessing the influence of air pollution on human well-being.

As, within the CNSLD categories, the associations found between air pollutants and respiratory symptoms are seen in grade 1 and more so in grade 2+3, the theory is supported that air pollutants - as exogenous stimuli - exert an effect via bronchial hyperreactivity (corresponding with a histamine hyperreactivity). Apart from the histamine hyperreactivity, there is the possibility of an existence of an individual sensitivity to air pollutants by a different mechanism. From experimental studies there is some evidence that an individual sensitivity exists to particulate matter, sulphur dioxide, and ozone.

Thirdly, also a pulmonary reaction pattern might be possible via preexisting pulmonary tissue damage, to which a predisposition of the individual is probably less important.

With regard to smoking there is only a slight indication that non-smokers and ex-smokers are more affected than smokers by high levels of air pollution with a time lag of 1 day and 2 days. It is noticeable that the associations between high levels of aldehydes and the symptoms are above all seen in the non-

smokers. An explanation for these findings might be: a self-selection of non-smokers as a result of being hyperreactive to exogenous stimuli, non-smokers producing less phlegm and having therefore a less sufficient defense mechanism, and smokers having adapted themselves more or less to exogenous stimuli. However, the results from experimental studies do not shed a conclusive light on this matter.

No appreciable relations of air pollutants to the peak flow have been found. This supports the initial query of whether lung function measurements once a week would be sufficient to reveal a possible association between changes in lung function and air pollution levels. In this context it is worth mentioning that Lawther et al. (1974^a, 1974^b, 1974^c) reported that day-to-day changes in ventilatory function measured by spirometry and peak flow were not so much related to environmental factors, but were affected more by respiratory infections, whose frequency is probably affected by exposure to air pollution (Douglas and Waller, 1966; Colley and Reid, 1970). In this study, however, this could not be confirmed.

Once more it should be stressed that an association found between a particular air pollutant and a symptom does not necessarily implicate a cause - effect relationship, because of the possibility that other unidentified factors - both in the environment and in the subjects - could have contributed to this association.

Desiderata.

The following items are worth considering and could be processed from this work.

- To apply a time series analysis to the data to detect associations between level of air pollution and symptoms, and using different time lags to this analysis.
- To study which individuals contributed most to the results, and to carry out further investigation in these individuals as regards the existence of an individual hyperreactivity or sensitivity.

- To analyze the data according to a no-yes answer system which will yield daily prevalences of the respiratory symptoms to compare with the point-prevalence data obtained in the (follow-up) studies that are carried out in Vlaardingen by the TNO Research Unit for Epidemiology.
- To study seasonal fluctuations of the prevalence of respiratory symptoms when having daily prevalence data available.
- To evaluate whether possible differences between Vlaardingen and Ommoord in health care, medical treatment, and socio-economic class could have influenced the results.

It is felt that sufficient data can be obtained from this work to instigate and advance further lines of study and investigation, in various directions.

SUMMARY

An epidemiological study was carried out in the Rijnmond area during one year (1973) in order to examine whether there is an association between high levels of urban air pollution and respiratory morbidity in this area.

The study population consisted of a random sample of women in the age-group 18-42 years in Vlaardingen, which town is polluted especially by the petrochemical industries in the Rijnmond area. To eliminate as far as possible the concomitant effects of meteorological conditions a control population was chosen in Ommoord, a relatively low polluted district of Rotterdam and situated close to Vlaardingen.

In Chapter I general aspects are given on air pollution, its nature and sources, and on the main air pollutants found in the urban atmosphere.

Chapter II gives a review of the literature on the effects of air pollution on the airways which served as background information for this study.

The *experimental studies on animals* have shown that most of the air pollutants commonly found in the urban atmosphere can exert adverse effects on the airways resulting in pathological changes and effects on the lung function. However, in most experiments such concentrations of air pollutants in combination with such exposure times were used as are likely never to be experienced by man in the urban environment.

The *experimental studies on man* have demonstrated that exposure to air pollutants can give rise to respiratory symptoms and to a decrement in the pulmonary function. The existence of an individual sensitivity to particulate matter, sulphur dioxide, and ozone is suggested. Especially persons with some degree of Chronic Non-Specific Lung Disease (CNSLD) seem to be sensitive to exposure to air pollutants. From the experimental studies

no consistent differences in reaction between smokers and non-smokers emerged.

The *epidemiological studies* on the effects of short-term exposures to high levels of urban air pollution have demonstrated that there is an association between acute and subacute episodes of high pollution, and both respiratory mortality and morbidity. With regard to the respiratory morbidity, both an increase in respiratory symptoms and a decrement in the pulmonary function have been found, especially in persons with a history of chronic obstructive pulmonary disease. It has been shown that long-term exposure to urban air pollution even more so together with other environmental factors can result in an increased prevalence of chronic obstructive pulmonary disease, especially in cigarette smokers.

In Chapter III the general aspects of the present epidemiological study in the Rijnmond area are discussed and the objectives of the study are presented.

The objectives were:

- a. To study whether there is an association between high levels of air pollution of short duration and an excess in respiratory morbidity, using respiratory symptoms and spirometric values as indices.
- b. To study whether persons with CNSLD differ from persons without CNSLD as regards the objective a.
- c. To study which air pollutant might be responsible for the effects found.

In this respect special reference is given to the definition and aetiology of Chronic Non-Specific Lung Disease, because the hypothesis has been postulated that air pollution is one of the non-specific exogenous stimuli that can cause bronchial obstruction and/or respiratory symptoms as a result of an existing hyperreactivity of the bronchus, which is one of the basic mechanisms in the aetiology of CNSLD.

In Chapter IV the methods of investigation are considered. Before the start of the investigation both the study population in Vlaardingen and the control population in Ommoord were sub-

divided into four groups according to degree of CNSLD (no CNSLD to severe CNSLD). The subdivision was based upon the answers to the TNO questionnaire on respiratory symptoms and upon spirometric values. Matched pairs were formed by the method of individual matching with respect to degree of CNSLD, smoking habit, and age. In this way, the effects of these confounding factors could be removed between the members of a pair. In total 396 pairs entered the study: 150 pairs in CNSLD grade 0 (no CNSLD), 128 pairs in CNSLD grade 1 (slight degree of CNSLD), 112 pairs in CNSLD grade 2 (moderate degree of CNSLD), and 6 pairs in CNSLD grade 3 (severe degree of CNSLD).

The day by day follow-up of respiratory symptoms was assessed by using a diary technique, and once a week a simple lung function test was carried out during a home visit. The home visits formed an essential part in arriving at an optimum cooperation of the women. The lung function test was done initially only with the Monaghan electronic spirometer, but later the Wright Peak Flow meter was also introduced.

Both in Vlaardingen and in Ommoord daily air pollution measurements were carried out for the purpose of this study on the following pollutants: standard smoke, sulphur dioxide, nitrogen monoxide, nitrogen dioxide, ozone, and aldehydes.

Chapter V deals with the presentation of the data and the method of statistical analysis. Because matched pairs were used, the analysis was carried out on the differences found between the Vlaardingen and Ommoord members of the pairs with respect to each of the symptoms and the lung function values. The data on the symptoms and the peak flow are shown as graphs in Appendix C. The air pollution data and the meteorological data are presented as graphs in the Appendices D and E. The actual values corresponding with the graphs are given in the TABLES.

Chapter VI presents the results of the investigation. During the whole year of investigation 105 individuals from the initial 792 individuals were lost. This caused a loss of 93 pairs which proved to be independent of degree of CNSLD. The cooperation of the women was extremely good.

The assumption which was made that the meteorological conditions in Vlaardingen and Ommoord were similar proved to be true as judged by the data on temperature and relative humidity in both places.

For the analysis a set of days were selected with contrastive air pollution levels in Vlaardingen and Ommoord for each pollutant separately (p. 102-106).

The significant associations found are presented in the tables 6.8. to 6.12. (p. 109-114).

In Chapter VII a general discussion is given of the study design, the analysis of the data, and the results. The discussion concludes with a summing-up of items remaining unsolved.

From this study the following conclusions can be drawn:

1. The diary technique during a whole year can be well applied provided that home visits are made regularly.
2. There is an association between high levels of air pollution of short duration and respiratory morbidity.
3. Mainly the photochemical pollutants nitrogen monoxide, ozone, and aldehydes are related to the symptoms.
4. Individuals with moderate to severe degree of CNSLD seem to be affected most.
5. High levels of air pollution of short duration exert an immediate "effect" mainly on the symptom irritation of the eyes, and a delayed "effect" mainly on the respiratory symptom cough.
6. There is a slight indication that non-smokers are more affected by high levels of air pollution of short duration than smokers.
7. Weekly peak flow values showed to be insufficient in demonstrating any associations with high levels of air pollution of short duration.

SAMENVATTING

Een epidemiologisch onderzoek werd uitgevoerd in het Rijnmond gebied gedurende het jaar 1973 om een mogelijk verband na te gaan tussen kortdurende pieken in de luchtverontreiniging en respiratoire morbiditeit in dit gebied.

De onderzoekpopulatie bestond uit een aselecte steekproef van vrouwen in de leeftijd van 18-42 jaar in Vlaardingen. Deze stad ondervindt veel hinder van luchtverontreiniging, voornamelijk veroorzaakt door de petrochemische industrieën in het Rijnmond gebied. Om de invloed van de weersomstandigheden zo veel mogelijk uit te kunnen schakelen werd een controlepopulatie van vrouwen geformeerd in Ommoord, een nieuwe buitenwijk van Rotterdam. Ommoord is in mindere mate aan luchtverontreiniging blootgesteld, terwijl de weersomstandigheden gelijk aan die in Vlaardingen kunnen worden beschouwd.

In Hoofdstuk I wordt een algemene beschouwing gegeven over luchtverontreiniging. De belangrijkste luchtverontreinigers die een rol spelen in de stedelijke luchtverontreiniging worden besproken.

Hoofdstuk II geeft een literatuuroverzicht met betrekking tot de effecten van luchtverontreiniging op de luchtwegen, dat diende als achtergrondinformatie voor dit onderzoek.

De experimentele onderzoeken bij dieren hebben aangetoond dat de meeste luchtverontreinigers, die gewoonlijk in de stedelijke buitenlucht worden aangetroffen, pathologische veranderingen van de luchtwegen teweeg kunnen brengen en effecten op de longfunctie. In de meeste dierexperimenten werden echter zeer hoge concentraties van luchtverontreinigers gebruikt met een zodanige lange expositieduur, dat het niet waarschijnlijk is dat de mens ooit aan zulke omstandigheden zal worden blootgesteld in het stedelijke milieu.

De experimentele onderzoeken bij mensen hebben aangetoond dat de luchtverontreinigers aanleiding kunnen geven tot klachten van de luchtwegen en tot een vermindering van de longfunctie. Er zijn aanwijzingen dat er een individuele gevoeligheid bestaat voor gewogen stof, zwaveldioxide en ozon. Vooral personen met Chronische Aspecifieke Respiratoire Aandoeningen (CARA) lijken gevoelig te zijn bij blootstelling aan luchtverontreinigers. Uit de experimentele onderzoeken komen geen consistente verschillen naar voren in reactie op de blootstelling aan luchtverontreinigers tussen personen die roken en personen die niet roken.

De epidemiologische onderzoeken naar de effecten van kortdurende pieken in de luchtverontreiniging hebben aangetoond dat er een verband bestaat tussen acute en subacute episoden van luchtverontreiniging aan de ene kant en respiratoire mortaliteit en morbiditeit aan de andere kant. Wat betreft de respiratoire morbiditeit, wordt zowel een toename van de respiratoire symptomen gevonden als ook een vermindering van de longfunctie, vooral bij personen met CARA. Bij langdurige blootstelling aan stedelijke luchtverontreiniging, vooral in combinatie met andere milieu factoren, blijkt dat er een toename kan optreden van de prevalentie van CARA, vooral bij personen die sigaretten roken.

In Hoofdstuk III worden de algemene aspecten besproken van het epidemiologische onderzoek in het Rijnmond gebied. De vragenstellingen van het onderzoek waren:

- a. Bestaat er een verband tussen pieken in de luchtverontreiniging en een toename van de respiratoire morbiditeit, waarbij gekeken werd naar respiratoire symptomen en longfunctie waarden.
- b. Verschillen personen met CARA van personen zonder CARA met betrekking tot dit verband.
- c. Kan er een bepaalde luchtverontreiniger verantwoordelijk gesteld worden voor de effecten die gevonden zijn.

Speciale aandacht wordt besteed aan de definitie en aetiologie van CARA, daar de hypothese aangenomen is, dat luchtverontrei-

niging één van de niet specifieke exogene prikkels is die aanleiding kan geven tot bronchusobstructie en/of respiratoire symptomen als gevolg van het bestaan van een overgevoeligheid van de bronchiaalboom, welke één van de basis mechanismen is in de aetiologie van CARA.

In Hoofdstuk IV worden de methoden van onderzoek besproken. De onderzoekpopulatie en de controlepopulatie werden, voor het onderzoek begon, ingedeeld in vier groepen naar ernst van CARA (geen CARA tot ernstige CARA). Deze indeling werd gebaseerd op de antwoorden op een aantal vragen van de gestandaardiseerde TNO questionnaire naar chronische longaandoeningen en op longfunctie waarden. Gebruik werd gemaakt van de methode der gepaarde controles, waarbij als relevante kenmerken graad van CARA, rookgewoonte en leeftijd werden beschouwd, teneinde de invloed van deze kenmerken binnen het paar uit te kunnen schakelen. In totaal startten 396 paren in het onderzoek: 150 paren in CARA graad 0 (geen CARA), 128 paren in CARA graad 1 (lichte CARA), 112 paren in CARA graad 2 (matige CARA) en 6 paren in CARA graad 3 (ernstige CARA).

Het dagelijks vervolgen van de respiratoire symptomen werd gedaan met behulp van dagboekjes, en eens per week werd een eenvoudige longfunctie test uitgevoerd tijdens huisbezoek. Het bezoeken van de vrouwen thuis was van wezenlijk belang om te komen tot een optimale medewerking van de vrouwen. Het longfunctie onderzoek werd aanvankelijk alleen met de Monaghan elektronische spirometer verricht, maar later ook met de Wright Peak Flow meter.

Zowel in Vlaardingen als in Ommoord werden speciaal voor dit onderzoek dagelijks de volgende luchtverontreinigers gemeten: standaard rook, zwaveldioxide, stikstofmonoxide, stikstofdioxide, ozon en aldehyden.

Hoofdstuk V betreft de presentatie van de gegevens en de methode van statistische analyse. Daar de methode der gepaarde controles was toegepast, werd de analyse uitgevoerd op de verschillen tussen de Vlaardingen en Ommoord leden van de paren met betrekking tot ieder symptoom afzonderlijk en de longfunctie

waarden. De gegevens van de symptomen en de peak flow worden als grafieken weergegeven in Appendix C. De gegevens van de luchtverontreiniging en de meteorologische gegevens worden als grafieken weergegeven in de Appendices D en E. De werkelijke waarden die corresponderen met deze gegevens worden getoond in de "TABLES".

Hoofdstuk VI beschrijft de resultaten van het onderzoek. Gedurende het jaar van onderzoek werden 105 personen verloren van de oorspronkelijke 792 personen. Dit veroorzaakte een verlies van 93 paren, op welk verlies de graad van CARA niet van invloed is geweest. De medewerking van de vrouwen was uitstekend. De veronderstelling dat de weersomstandigheden in Vlaardingen en Ommoord dezelfde zouden zijn, bleek gerechtvaardigd gezien de gegevens betreffende de temperatuur en relatieve vochtigheid, die van beide plaatsen verkregen werd.

Voor de analyse werd een groep dagen geselecteerd met tegengestelde luchtverontreinigingsniveaus in Vlaardingen en Ommoord, voor iedere luchtverontreiniger afzonderlijk (p. 102-106). De significante associaties die gevonden werden, worden weergegeven in tabel 6.8. tot en met tabel 6.12. (p. 109-114).

In Hoofdstuk VII wordt een algehele discussie gegeven betreffende de opzet van het onderzoek, de analyse van de gegevens en de resultaten. De discussie besluit met een opsomming van items die voor verdere analyse in aanmerking kunnen komen. Uit dit onderzoek kunnen de volgende conclusies getrokken worden:

1. Een dagboekjesonderzoek gedurende een geheel jaar kan met succes worden toegepast, mits regelmatig huisbezoek plaatsvindt.
2. Er is een verband tussen pieken in de luchtverontreiniging en respiratoire morbiditeit.
3. Voornamelijk de photochemische luchtverontreinigers stikstofmonoxide, ozon en aldehyden tonen een verband met de respiratoire symptomen en prikkeling van de ogen.
4. Personen met een matige tot ernstige graad van CARA lijken het meest gevoelig te zijn bij blootstelling aan luchtveront-

reiniging met betrekking tot de respiratoire symptomen.

5. Pieken in de luchtverontreiniging geven een onmiddellijk "effect" met name op het symptoom prikkeling van de ogen, en een vertraagd "effect" met name op het symptoom hoesten.
6. Er is een lichte aanwijzing dat personen die niet roken meer worden aangedaan door pieken in de luchtverontreiniging dan personen die roken.
7. De wekelijkse peak flow waarden bleken niet geschikt om enige associatie aan te tonen tussen pieken in de luchtverontreiniging en een vermindering van de longfunctie.

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APPENDIX A

CONVERSION TABLES

1. Introduction.

The conversion from e.g. parts per million (ppm) to milligrams per cubic meter (mg/m^3) can be derived as follows:

Example: ozone (O_3)

$$\begin{aligned} 1 \text{ ppm ozone} &= 1 \text{ liter ozone per } 10^6 \text{ liter (of air)} \\ &= 10^{-3} \text{ liter ozone per } 10^3 \text{ liter} \\ &= 10^{-3} \text{ liter ozone per m}^3 \quad (1) \end{aligned}$$

As 1 mole has a volume of

$$22.4 \times \frac{273 + \text{degrees centigrade (C)}}{273} \text{ liter (at 1 atmosphere)}$$

$$\text{hence, 1 liter ozone} = \frac{1 \text{ mole ozone}}{22.4 \times \frac{273 + C}{273}} \quad (2)$$

Consequently, from (1) and (2):

$$1 \text{ ppm ozone} = \frac{10^{-3} \text{ mole ozone}}{22.4 \times \frac{273 + C}{273}} \text{ per m}^3$$

As 1 mole ozone has a molecular weight of 48 grams ($\text{O} = 16$):

$$1 \text{ ppm ozone} = \frac{10^{-3} \times 48}{22.4 \times \frac{273 + C}{273}} \text{ g/m}^3 \text{ ozone}$$

For 25 degrees centigrade at 1 atmosphere:

$$1 \text{ ppm ozone} = \frac{10^{-3} \times 48}{22.4 \times \frac{298}{273}} \text{ g/m}^3 = 0.001963 \text{ g/m}^3 = 1.963 \text{ mg/m}^3 = 1963 \text{ } \mu\text{g/m}^3 \text{ ozone}$$

The general formulae:

$$1 \text{ ppm} = \frac{\text{molecular weight}}{22.4 \times \frac{273 + C}{273}} \text{ mg/m}^3$$

$$1 \text{ mg/m}^3 = \frac{22.4 \times \frac{273 + C}{273}}{\text{molecular weight}} \text{ ppm}$$

2. Conversion table of ppm to mg/m^3 and mg/m^3 to ppm for sulphur dioxide¹⁾ (at 25 degrees centigrade and 1 atmosphere).

ppm to mg/m^3		mg/m^3 to ppm	
0.05 ppm =	0.145 mg/m^3	0.100 mg/m^3 =	0.034 ppm
0.1 ppm =	0.290 mg/m^3	0.250 mg/m^3 =	0.085 ppm
0.2 ppm =	0.580 mg/m^3	0.500 mg/m^3 =	0.170 ppm
0.3 ppm =	0.870 mg/m^3	0.750 mg/m^3 =	0.255 ppm
0.4 ppm =	1.16 mg/m^3	1 mg/m^3 =	0.340 ppm
0.5 ppm =	1.45 mg/m^3	1.5 mg/m^3 =	0.510 ppm
1 ppm =	2.9 mg/m^3	5 mg/m^3 =	1.7 ppm
2.5 ppm =	7.2 mg/m^3	10 mg/m^3 =	3.4 ppm
5 ppm =	14.5 mg/m^3	50 mg/m^3 =	17 ppm
10 ppm =	29 mg/m^3	100 mg/m^3 =	34 ppm
50 ppm =	145 mg/m^3	200 mg/m^3 =	68 ppm
100 ppm =	290 mg/m^3	300 mg/m^3 =	102 ppm

¹⁾ Molecular weight of sulphur dioxide: 64 (32 + 2 x 16)

3. Conversion table of ppm to mg/m^3 and mg/m^3 to ppm for nitrogen dioxide¹⁾ (at 25 degrees centigrade and 1 atmosphere).

ppm to mg/m^3		mg/m^3 to ppm	
0.1 ppm =	0.188 mg/m^3	0.100 mg/m^3 =	0.05 ppm
0.5 ppm =	0.94 mg/m^3	0.500 mg/m^3 =	0.27 ppm
1 ppm =	1.88 mg/m^3	1 mg/m^3 =	0.53 ppm
2 ppm =	3.76 mg/m^3	5 mg/m^3 =	2.66 ppm
5 ppm =	9.4 mg/m^3	10 mg/m^3 =	5.32 ppm
10 ppm =	18.8 mg/m^3	20 mg/m^3 =	10.6 ppm
25 ppm =	47 mg/m^3	50 mg/m^3 =	26.6 ppm
50 ppm =	94 mg/m^3	100 mg/m^3 =	53.2 ppm
100 ppm =	188 mg/m^3	200 mg/m^3 =	106.4 ppm

¹⁾ Molecular weight of nitrogen dioxide: 46 (14 + 2 x 16)

4. Conversion table of ppm to mg/m^3 and mg/m^3 to ppm for ozone¹⁾ (at 25 degrees centigrade and 1 atmosphere).

ppm to mg/m^3		mg/m^3 to ppm	
0.05 ppm =	0.098 mg/m^3	0.100 mg/m^3 =	0.051 ppm
0.10 ppm =	0.196 mg/m^3	0.250 mg/m^3 =	0.128 ppm
0.25 ppm =	0.490 mg/m^3	0.500 mg/m^3 =	0.255 ppm
0.37 ppm =	0.725 mg/m^3	0.750 mg/m^3 =	0.382 ppm
0.50 ppm =	0.980 mg/m^3	1 mg/m^3 =	0.510 ppm
0.75 ppm =	1.47 mg/m^3	1.5 mg/m^3 =	0.765 ppm
1 ppm =	1.96 mg/m^3	2 mg/m^3 =	1.02 ppm
2.5 ppm =	4.9 mg/m^3	5 mg/m^3 =	2.55 ppm
5 ppm =	9.8 mg/m^3	10 mg/m^3 =	5.1 ppm

¹⁾ Molecular weight of ozone: 48 (3 x 16)

APPENDIX B-1

THE T.N.O. QUESTIONNAIRE ON RESPIRATORY SYMPTOMS.

GEZONDHEIDSORGANISATIE T.N.O. BEVOLKINGSONDERZOEK NAAR CHRONISCHE LONGAANDOENINGEN

Naam:	No.:		1, 2, 3, 4
Adres:	Geslacht:		5
Woonplaats:	Burg. staat:		6
Geboortedatum:	Leeftijd:		7, 8
Datum van het onderzoek	19	Dag:	
Uur van het onderzoek	Uur:		10
Enqueteur	Code no. enqueteur:		11, 12

Klachten

A Anamnese

Inleiding: Ik ga u een aantal vragen stellen, die betrekking hebben op uw borst. Wilt u hierop zoveel mogelijk met „ja” of „neen” antwoorden? Als een vraag niet duidelijk is, zegt u het me dan.

I Hoesten

- Hoest u 's winters **gewoonlijk** bij het opstaan?
(Hoesten bij de eerste sigaret, of bij het naar buiten gaan, als positief aanmerken. Geen nota nemen van „keelschrappen” of een enkele kich).
- Hoest u 's winters **gewoonlijk** overdag - of 's nachts? -
(Geen nota nemen van sporadisch hoesten)
Alleen indien minstens één der voorgaande vragen met „ja” wordt beantwoord vraag 3 en 4 stellen:
- Hoest u **zo** vrijwel dagelijks, wel drie maanden per jaar?
- Op welke leeftijd bent u begonnen te hoesten?

II Sputum

- Geeft u 's winters **gewoonlijk** bij het opstaan fluimen op?
(Opgeven van fluimen bij de eerste sigaret, of bij het naar buiten gaan, als positief aanmerken. Doorgeslipte fluimen meetellen. Geen nota nemen van sereet uit de neus-keelholte).
- Geeft u 's winters **gewoonlijk** overdag - of 's nachts - fluimen op?
(Vanaf 2 fluimen per dag noteren).
Alleen indien minstens één der voorgaande vragen met „ja” wordt beantwoord vraag 7 en 8 stellen:
- Geeft u **zo** vrijwel dagelijks fluimen op, wel drie maanden per jaar?
- Op welke leeftijd is het opgeven van fluimen begonnen?
- Heeft u in de afgelopen 3 jaren wel eens een periode gehad van (een toename van)** hoesten en opgeven van fluimen, die minstens 3 weken duurde?
Indien deze vraag met „ja” wordt beantwoord:
- Heeft u dit vaker dan één keer gehad?

* Codering: zie instructies

** Deze formulering gebruiken voor personen die gewoonlijk hoesten en fluimen opgeven

III Kortademigheid

(De vragen hebben betrekking op de doorsnee toestand van de onderzochte persoon in de winter).

- 11 Hier een „1“ invullen, wanneer de onderzochte persoon door een andere oorzaak dan hart- of longziekten moeilijkheden ondervindt bij het lopen.

25

ja neen

1

- 12 Heeft u last van kortademigheid, wanneer u zich op vlak terrein moet haasten, of wanneer u een lichte helling, of een trap in normale pas oploopt?
(„neen“ - graad 1, „ja“ - doorgaan)

ja neen

2

- 13 Heeft u last van kortademigheid, wanneer u met andere mensen van uw leeftijd in normaal tempo op vlak terrein loopt?
(„neen“ - graad 2, ga naar vraag 16, „ja“ - doorgaan)

ja neen

3

- 14 Moet u wel eens stilstaan om op adem te komen, wanneer u in uw eigen tempo op vlak terrein wandelt?
(„neen“ - graad 3, ga naar vraag 16, „ja“ - doorgaan)

ja neen

4

- 15 Bent u in rust kortademig?
(„neen“ - graad 4, ga naar vraag 16, „ja“ - doorgaan)

soms altijd

5 6

- 15a Soms of altijd?

Codering * 26

- 16 Op welke leeftijd heeft u bemerkt dat u kortademig was?
(Het antwoord is aanvaardbaar, indien met „rond deze leeftijd“ wordt geantwoord).

2 cijfers jr.
 27, 28

IV Piepende ademhaling

- 17 Heeft u ooit last van „piepen op de borst“ gehad?

ja neen

1

Zo ja:

- 18 Heeft u dit de meeste dagen of nachten?

ja neen

2

Zo ja:

- 18a Heeft u dit vrijwel alle dagen of nachten?

ja neen

3

Codering * 29

V Astma aanvallen

- 19 Heeft u wel eens in rust aanvallen van benauwdheid met „piepen op de borst“ gehad? (Astma-aanvallen)

ja neen
 30
1 2

Zo ja:

- 20 Op welke leeftijd heeft u de eerste aanval gehad?
(Het antwoord is aanvaardbaar, indien met „rond deze leeftijd“ wordt geantwoord).

2 cijfers jr.
 31, 32

- 21 Op welke leeftijd heeft u de laatste aanval gehad?
(Het antwoord is aanvaardbaar, indien met „rond deze leeftijd“ wordt geantwoord).

2 cijfers jr.
 33, 34

VI Invloed van het weer

- 22 Heeft het weer invloed op uw ademhaling?
(Hoest, opgeven van fluimen, piepen op de borst, kortademigheid).
(Als „ja“ te aanvaarden, indien bepaalde weersomstandigheden duidelijk en geregeld invloed hebben).

ja neen
 35
1 2

* Codering: zie instructies.

VII Neuscatarrh

- 23 Heeft u **gewoonlijk** last van een verstopte neus of van een loopneus?

Zo ja:

ja	neen	
☐	☐	36
1	2	

- 24 Heeft u dit vrijwel dagelijks, wel drie maanden per jaar?

ja	neen	
☐	☐	37
1	2	

- 25 Heeft u last van „hooikoorts“ (gehad)?

(Alleen te aanvaarden typische gevallen samengaand met seizoen-gebonden allergenen).

ja	neen	
☐	☐	38
1	2	

VIII Ziekten van de luchtwegen

- 26 Heeft u de laatste 3 jaren een ziekte van de luchtwegen gehad, waardoor u uw gewone werkzaamheden gedurende minstens een week niet kon verrichten?

ja	neen	
☐	☐	1

Zo ja:

- 27 Gaf u daarbij meer fluimen op dan gewoonlijk?

ja	neen	
☐	☐	2

Zo ja:

- 28 Hoeveel van dergelijke perioden heeft u in de laatste 3 jaren gehad?

1 per.	☐	3
--------	--------------------------	---

2 per. of meer.	☐	4
-----------------	--------------------------	---

Codering * ☐ 39

- 29 Heeft u ooit één of meer van de volgende aandoeningen gehad:

a (+) een ongeluk of een operatie aan uw borstkas?

☐	40
--------------------------	----

b (+) een hartaandoening?

☐	41
--------------------------	----

c (+) een hartklepaandoening?

☐	42
--------------------------	----

d (+) verhoogde bloeddruk?

☐	43
--------------------------	----

e (+) een nieraandoening?

☐	44
--------------------------	----

f (x) bronchitis?

☐	45
--------------------------	----

g (x) longontsteking?

☐	46
--------------------------	----

h (x) pleuritis?

☐	47
--------------------------	----

i (+) longtuberculose?

☐	48
--------------------------	----

j (x) andere borstaandoeningen?

☐	49
--------------------------	----

(+) Codering 0 = neen 1 = ja

(x) Codering 0 = neen 1 = 1 x 2 = 2 x

3 = 3 x, 4, 5 enz.... 9 = 9 x of meer.

Gaarne nadere precisering bij ieder positief antwoord.

IX Roken

- 30 Rookt u?

ja	neen	
☐	☐	50
1	2	

- 30a Heeft u vroeger gerookt?

ja	neen	
☐	☐	51
1	2	

- 31 Op welke leeftijd bent u begonnen geregeld te roken?

2 cijfers		jr.	52, 53
-----------	----------------------	-----	--------

* Codering: zie instructies.

31a

Tabel

	Fabrieks- sigaretten gemiddeld per dag	Gerolde sigaretten gemiddeld per dag	Sigaren gemiddeld per week	Cigarillos gemiddeld per week	Pijp- tabak/gr gemiddeld per week	Inha- latie		
nu *								54, 55, 56
de laatste 10 jr. *								57, 58, 59
daarvoor *								60, 61, 62
32 Indien u het roken gestaakt heeft, hoe lang is dat geleden?*								63
33 Indien u het roken verminderd of gestaakt heeft, is dat dan gebeurd wegens borstklachten?							ja neen	64
							1 2	65 t/m 74
Reserve codering *								75, 76
Volg no. onderzoek *								77, 78, 79, 80
Coderingsruimte A.B.W. *								1 ^{II} , 2 ^{II} , 3 ^{II} , 4 ^{II}
Herhaling persoons no. *								

X Beroepsanamnese

34 Wat is uw huidige beroep? Hoelang heeft u dat uitgeoefend? Welke beroepen heeft u daarvoor gehad? Hoelang?

a Codering: huidige beroep en duur *

b Codering: beroep dat hiervóór gedurende minstens 6 maanden werd uitgeoefend en duur *

c Codering: voornaamste beroep, dat vroeger werd uitgeoefend vóór b en duur *

37 Komt of kwam u beroepshalve in aanraking met chemische dampen, prikkelende gasen, stof of rook?*

39 Krijgt u borstklachten (verergeren uw borstklachten)** door gasen, stof, rook of dampen tijdens uw huidige werkzaamheden?* Was dit bij uw vorige werkzaamheden het geval?*

42 Welke opleiding heeft u gehad?*

43 Omschrijving van de huidige werkzaamheden

Opmerkingen van de vragensteller wat betreft de risico's van de huidige en vroegere werkzaamheden

B Fysisch onderzoek:	a Piepende of brommende ronchi	ja neen	19 ^{II}
		1 2	
	b Vochtige ronchi	ja neen	20 ^{II}
		1 2	
	c Verlengd expirium	ja neen	21 ^{II}
		1 2	
	Herhaling volg no. onderzoek		75 ^{II} , 76 ^{II}

* Codering: zie instructies.

** Formulering afhankelijk van het al of niet bestaan van borstklachten.

APPENDIX B-2

DIAGNOSTIC CRITERIA FOR THE DIFFERENT GRADES OF CNSLD.

- GRADE 0: *no respiratory symptoms*: a clear "no" answer to question 3 (persistent cough), question 7 (persistent phlegm), question 9 (at least one chest illness), question 12 (dyspnoea), question 17 (wheezing), and question 19 (asthmatic attacks) of the TNO questionnaire on respiratory symptoms,
and
no impairment of the lung function, i.e. $FEV_{1,0}\%VC$ not more than 10% below the predicted value.
- GRADE 1: *respiratory symptoms*: a clear "yes" answer to one or more of the following questions of the TNO questionnaire on respiratory symptoms:
persistent cough (question 3),
persistent phlegm (question 7),
one chest illness ("yes" to question 9, "no" to question 10),
dyspnoea grade II ("yes" to question 12, "no" to question 13),
wheezing grade II ("yes" to question 17, "no" to question 18),
and
a clear "no" answer to question 19 (asthmatic attacks),
and
no impairment of the lung function, i.e. $FEV_{1,0}\%VC$ not more than 10% below the predicted value.

Exception: If dyspnoea grade II will be found in combination with two or more "yes" answers to the above mentioned questions, this combination is placed in grade 2.
- GRADE 2: *respiratory symptoms*:
a. a clear "yes" answer to one or more of the following questions of the TNO questionnaire on respiratory symptoms:
more than one chest illness (question 9 and 10),
dyspnoea grade III (question 13),
wheezing grade III (question 18),
asthmatic attacks (question 19).
b. all other combinations, that do not fulfil the criteria of grade 1 and 3,
and/or
slight to moderate impairment of the lung function, i.e. $FEV_{1,0}\%VC$ 10-20% below the predicted value.
- GRADE 3: *respiratory symptoms*:
a "yes" answer to *all* of the following questions of the TNO questionnaire on respiratory symptoms:
persistent cough (question 3),
persistent phlegm (question 7),
more than one chest illness (question 9 and 10),
dyspnoea grade III (question 13),
wheezing grade III (question 18),
asthmatic attacks (question 19),
and/or
moderate to severe impairment of the lung function, i.e. $FEV_{1,0}\%VC$ more than 20% below the predicted value.

APPENDIX C

FIGURES C 1 TO 5 SHOWING THE DAILY MEAN SCORE-DIFFERENCES BETWEEN VLAARDINGEN AND OMMOORD FOR THE RESPIRATORY SYMPTOMS AND IRRITATION OF THE EYES, ACCORDING TO DEGREE OF CNSLD.

FIGURE C 6 SHOWING THE DAILY MEAN OF THE DIFFERENCES IN "PERCENTAGE DIFFERENCE FROM THE MEAN" BETWEEN VLAARDINGEN AND OMMOORD FOR THE PEAK FLOW VALUES, ACCORDING TO DEGREE OF CNSLD.

FIG. C 1. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *cough* ACCORDING TO DEGREE OF CNSLD.

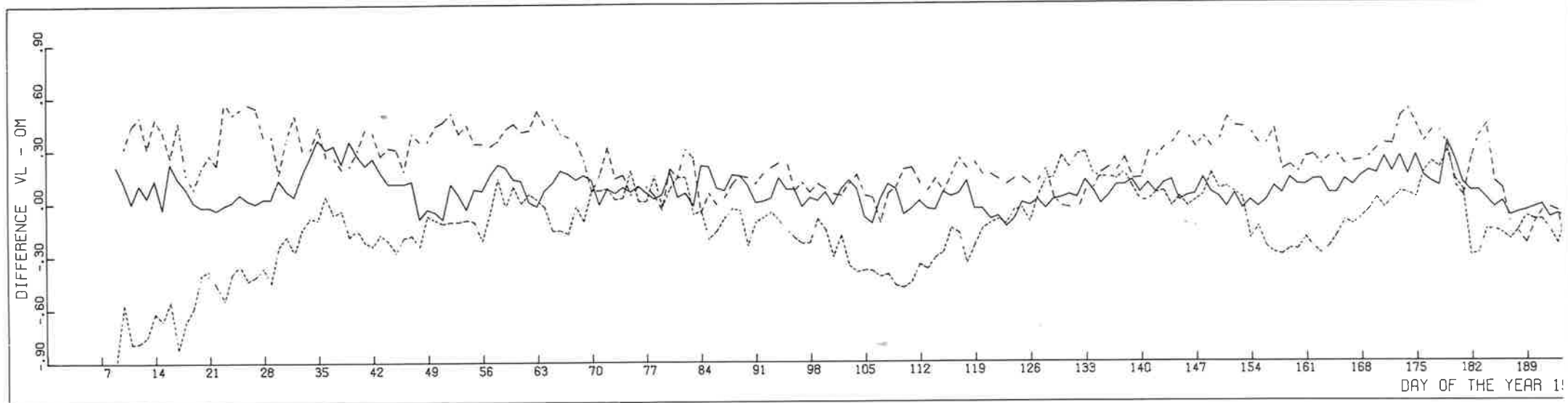
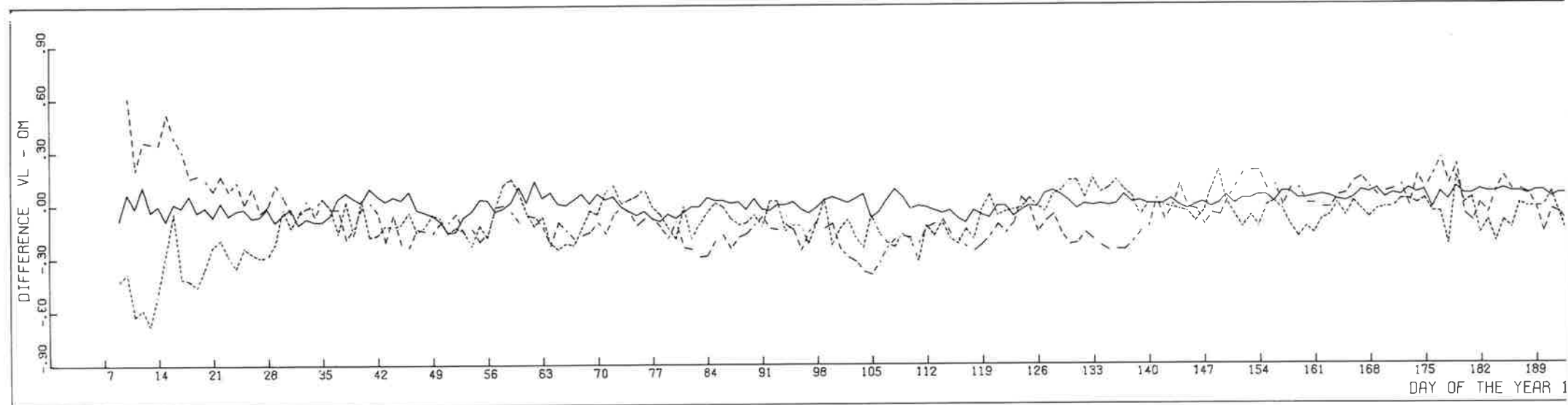


FIG. C 2. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *phlegm* ACCORDING TO DEGREE OF CNSLD.



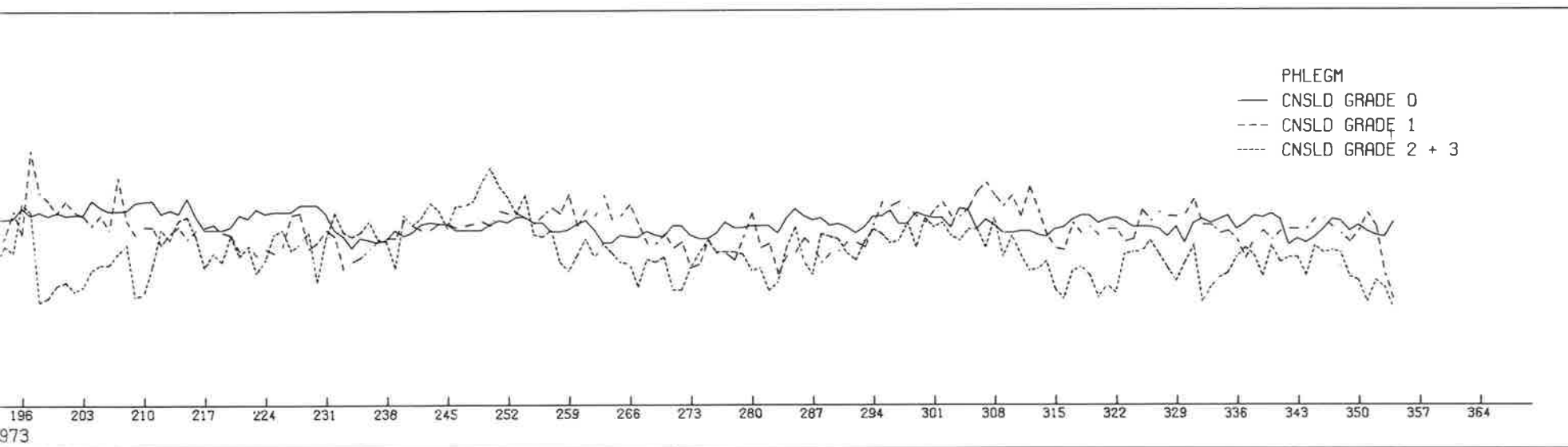
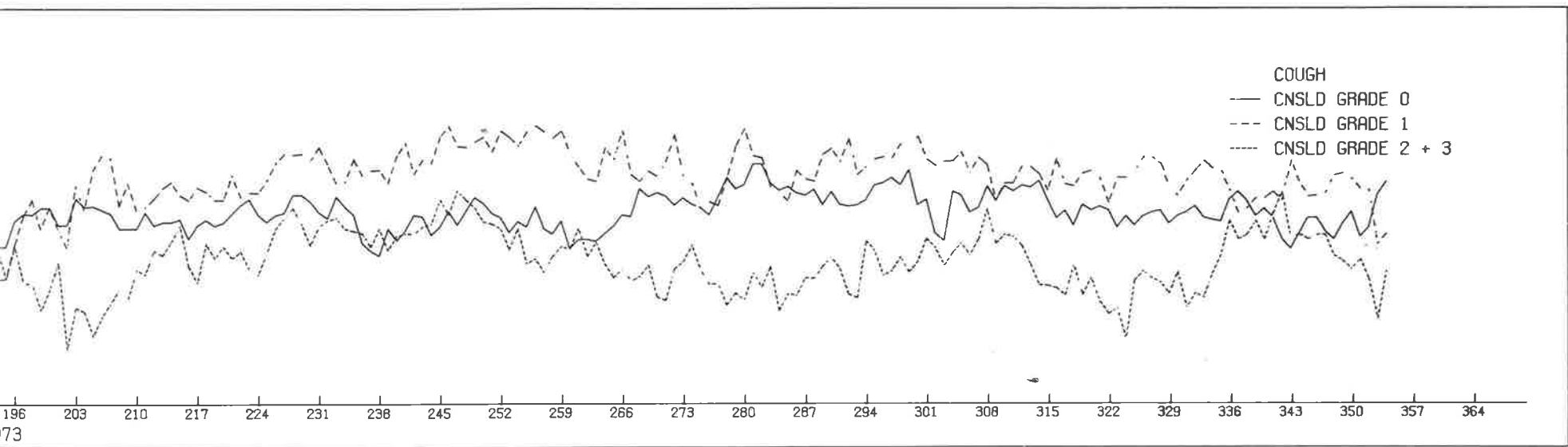


FIG. C 3. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *dyspnoea* ACCORDING TO DEGREE OF CNSLD.

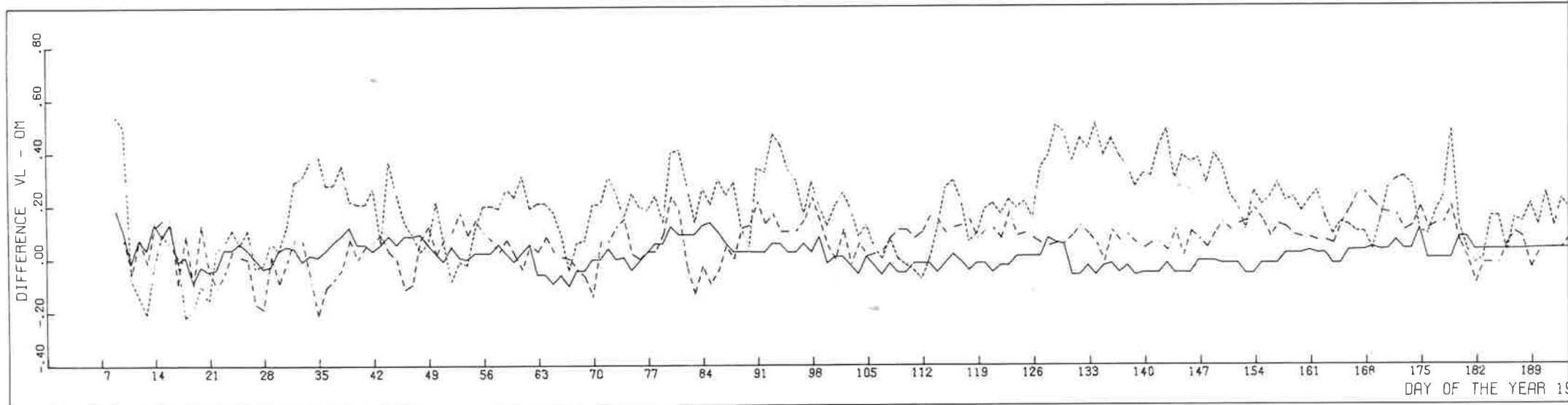
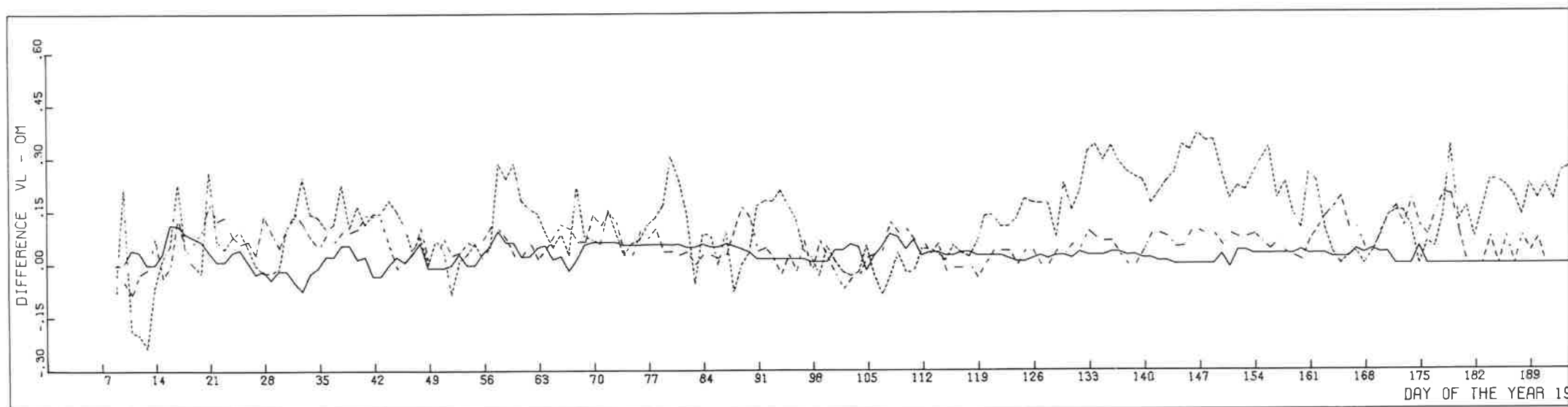


FIG. C 4. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *wheezing* ACCORDING TO DEGREE OF CNSLD.



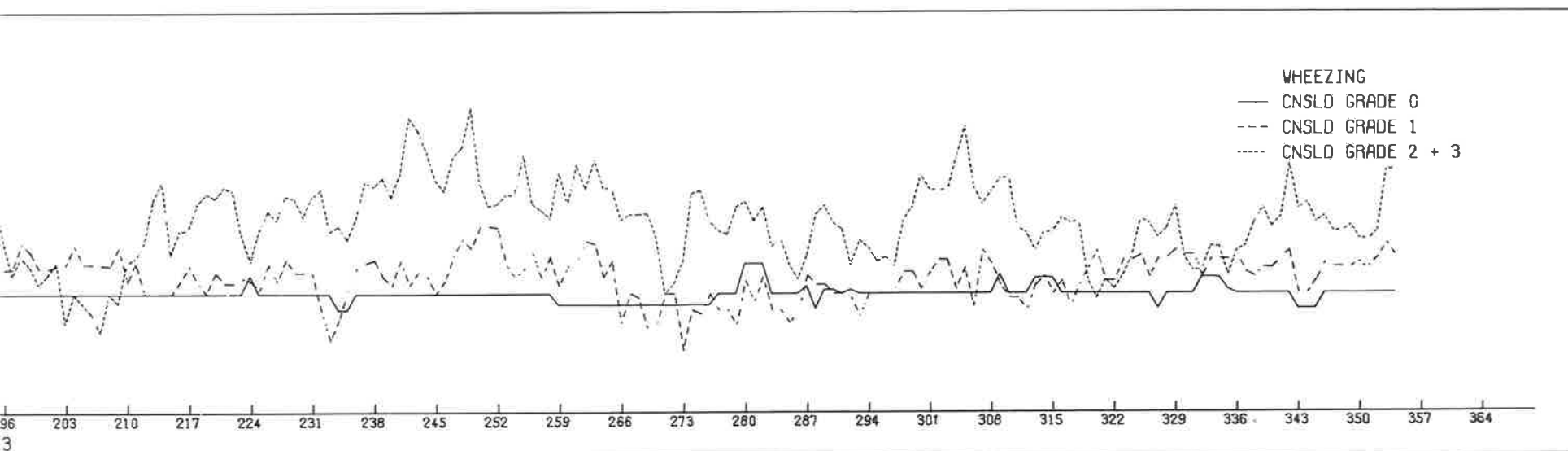
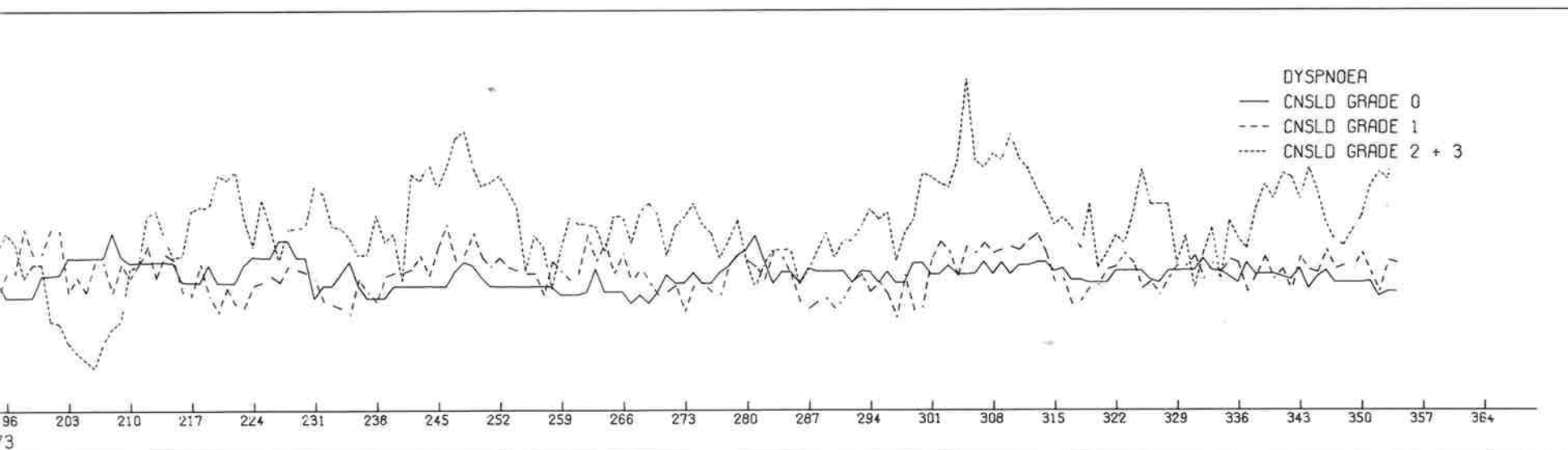


FIG. C 5. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *irritation of the eyes* ACCORDING TO DEGREE OF CNSLD.

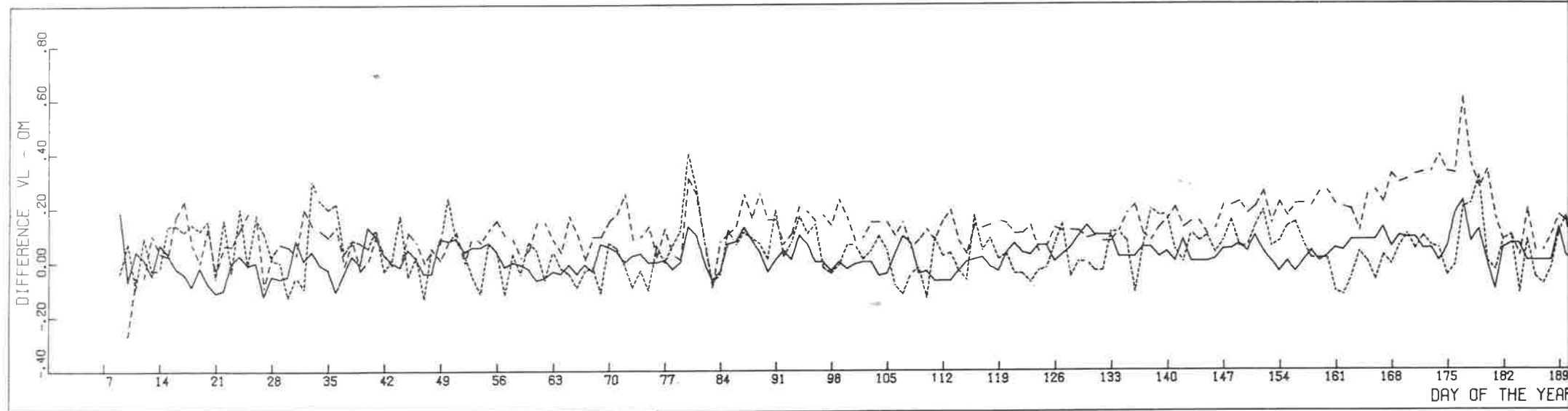
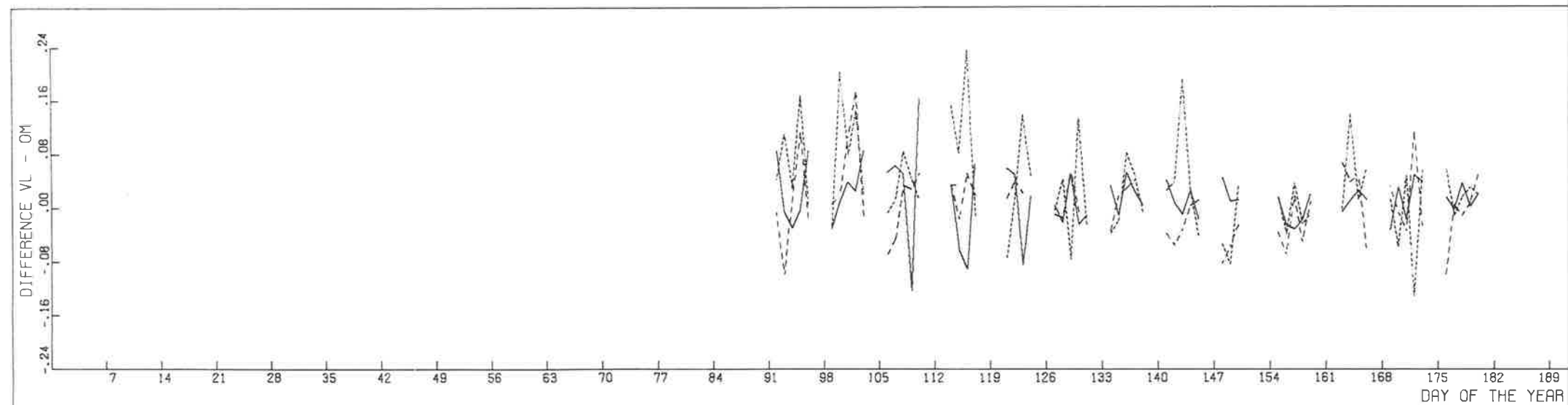
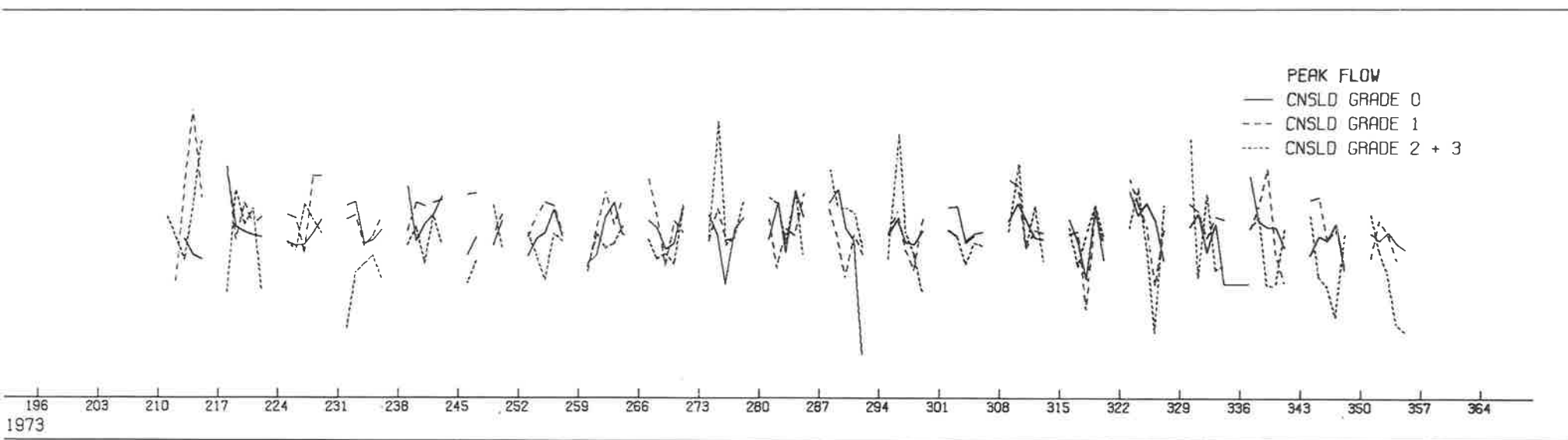
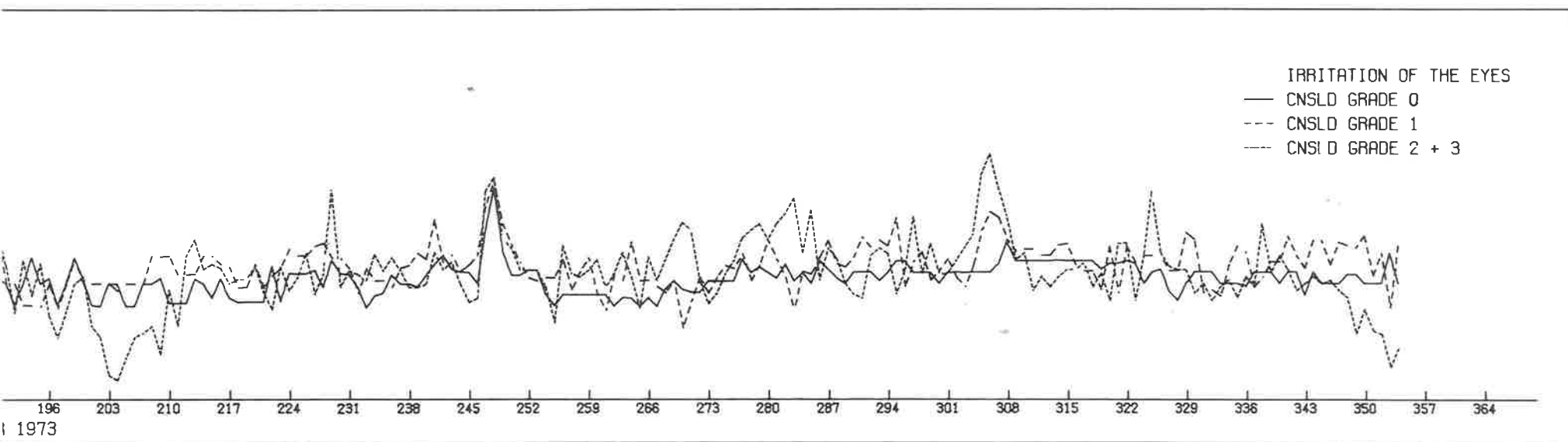


FIG. C 6. THE DAILY MEAN OF THE DIFFERENCES IN "PERCENTAGE DIFFERENCE FROM THE MEAN" WITH RESPECT TO THE *peak flow values* ACCORDING TO DEGREE OF CNSLD.





APPENDIX D

FIGURES D 1 TO 10 SHOWING THE DAILY CONCENTRATIONS OF THE AIR POLLUTANTS IN VLAARDINGEN AND OMMOORD.

FIG. D 1. THE 24-hour average CONCENTRATION OF *sulphur dioxide* IN VLAARDINGEN AND OMMOORD (IN MICROGRAMS/M³).

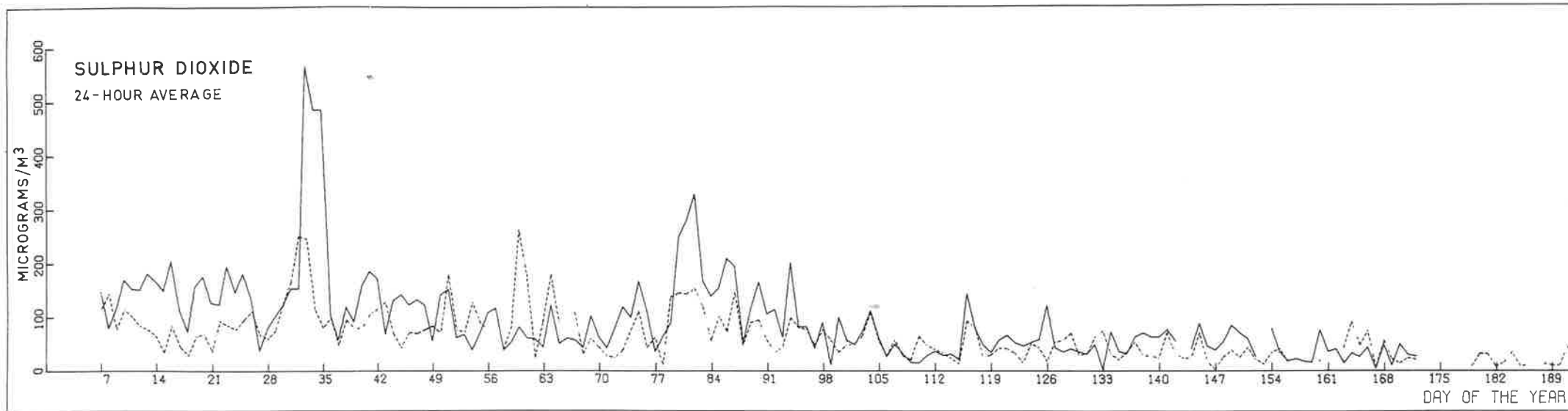
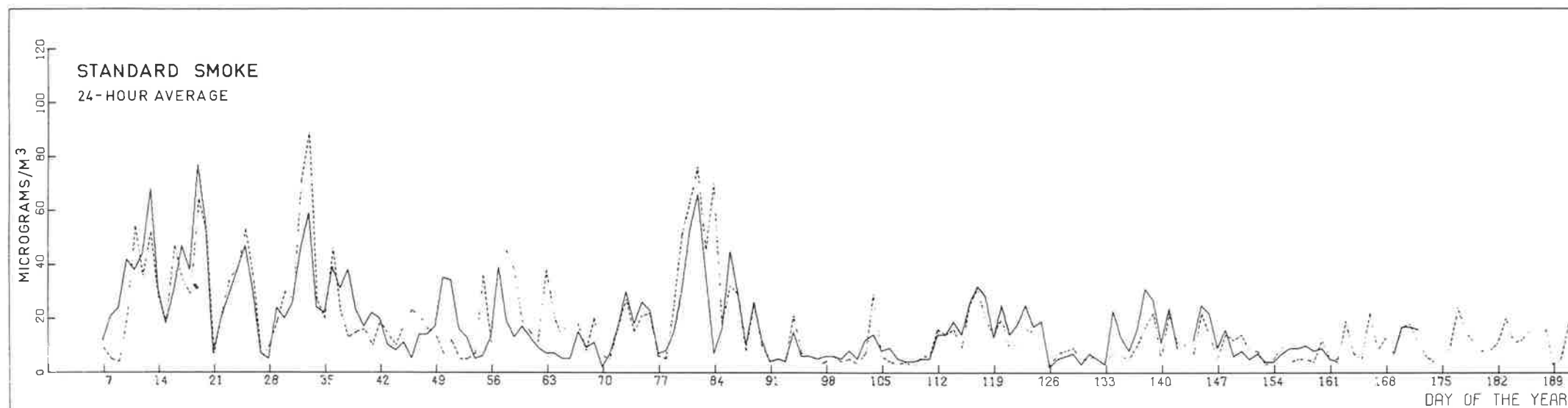


FIG. D 2. THE 24-hour average CONCENTRATION OF *standard smoke* IN VLAARDINGEN AND OMMOORD (IN MICROGRAMS/M³).



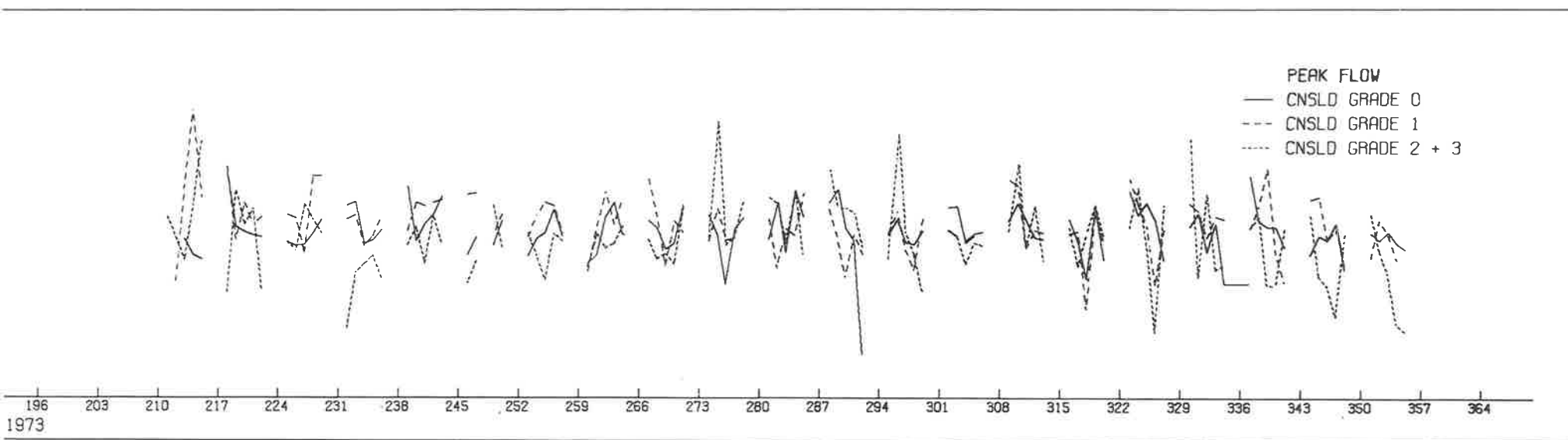
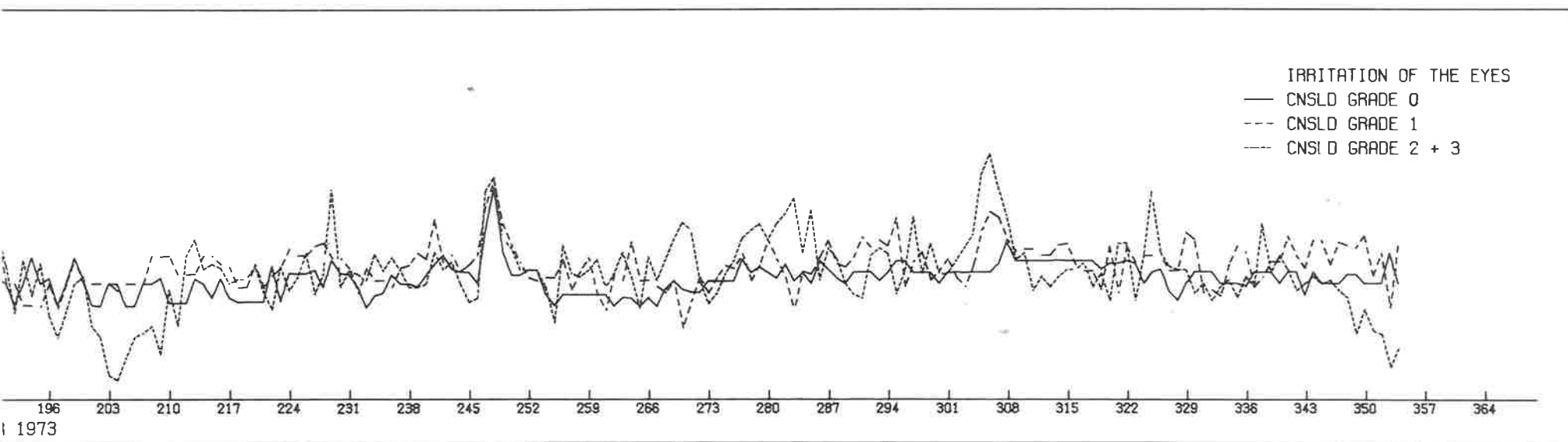


FIG. D 1. THE 24-hour average CONCENTRATION OF *sulphur dioxide* IN VLAARDINGEN AND OMMOORD (IN MICROGRAMS/M³).

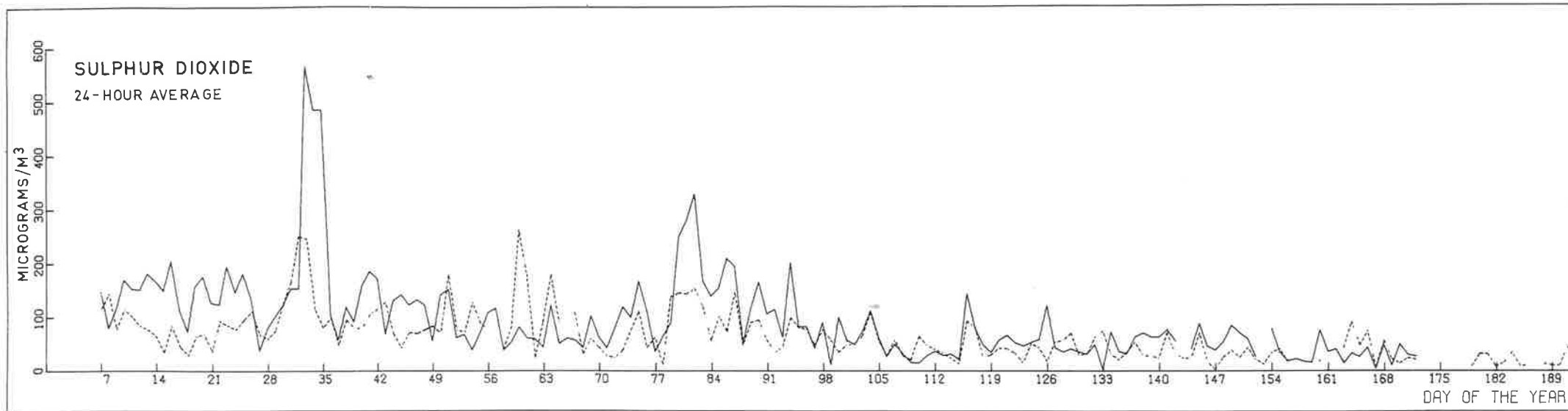
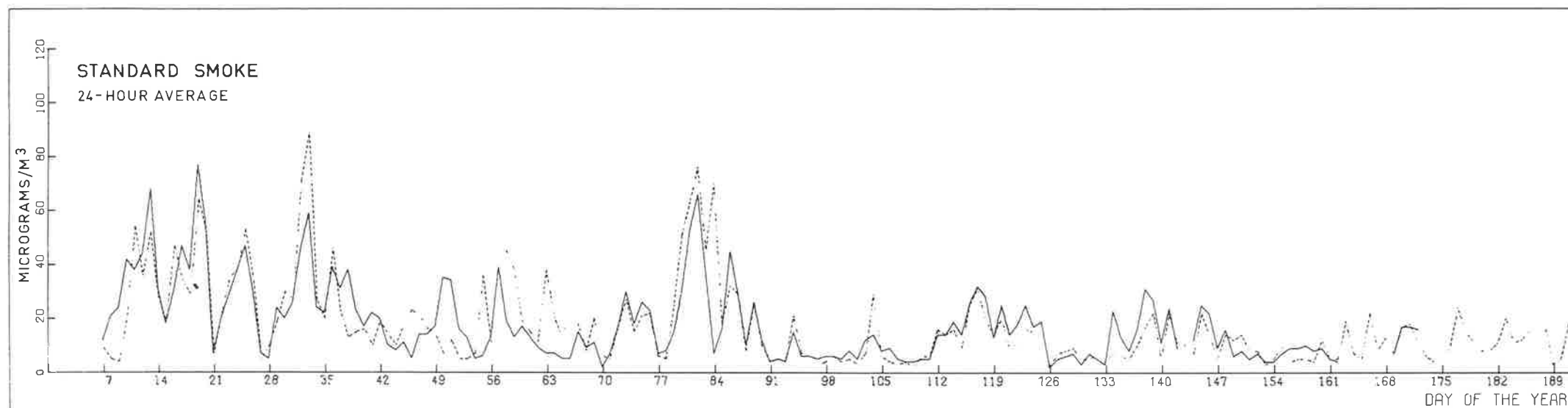


FIG. D 2. THE 24-hour average CONCENTRATION OF *standard smoke* IN VLAARDINGEN AND OMMOORD (IN MICROGRAMS/M³).



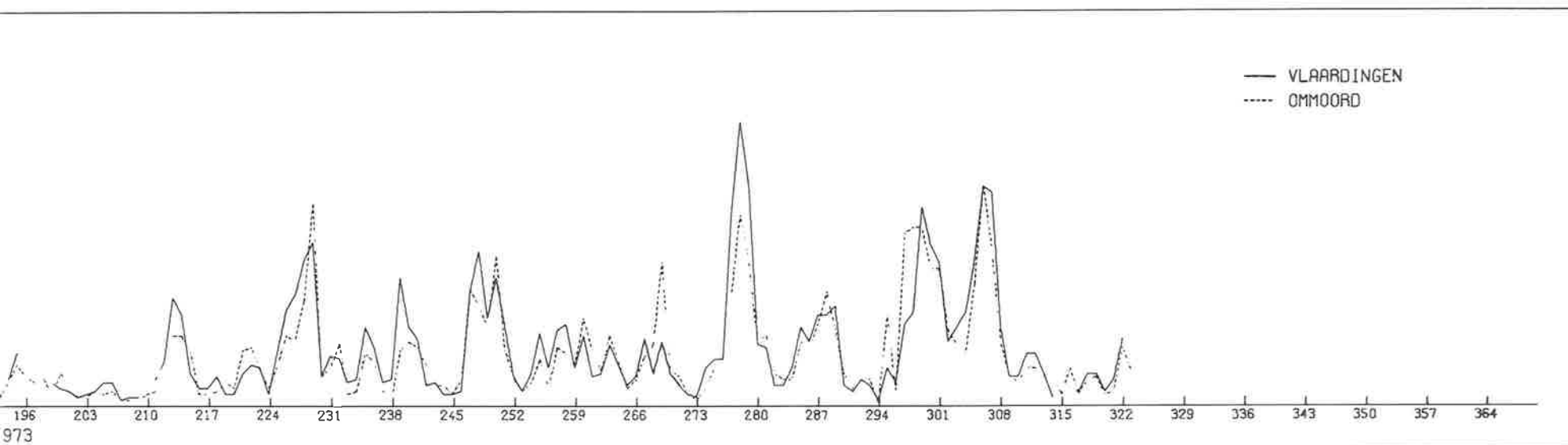
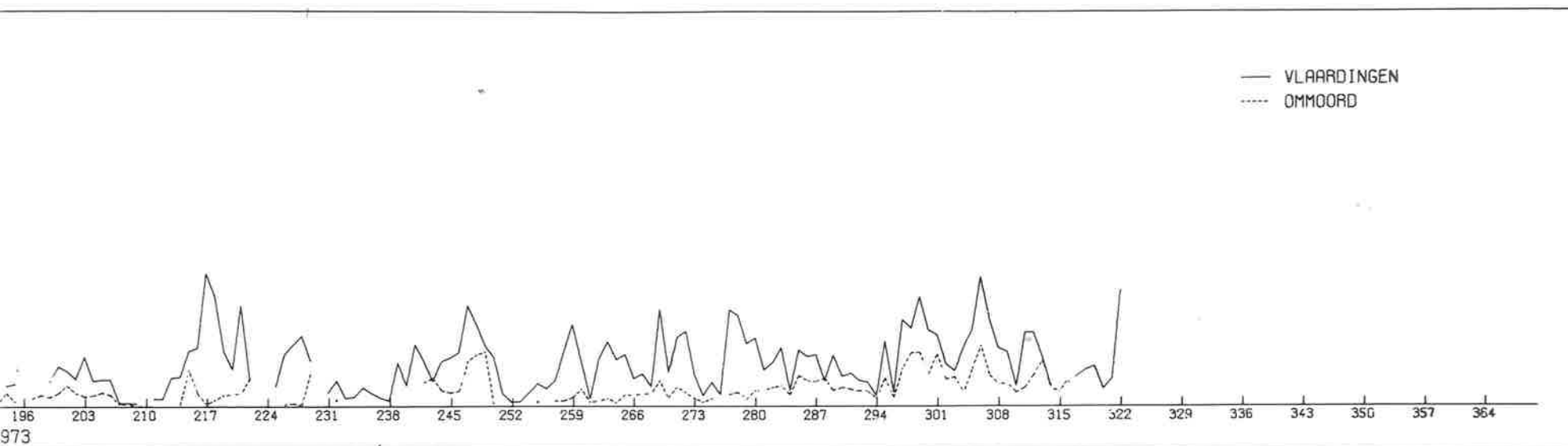


FIG. D 3. THE *daily average* CONCENTRATION OF *nitrogen monoxide*
IN VLAARDINGEN AND OMMOORD (IN MICROGRAMS/M³).

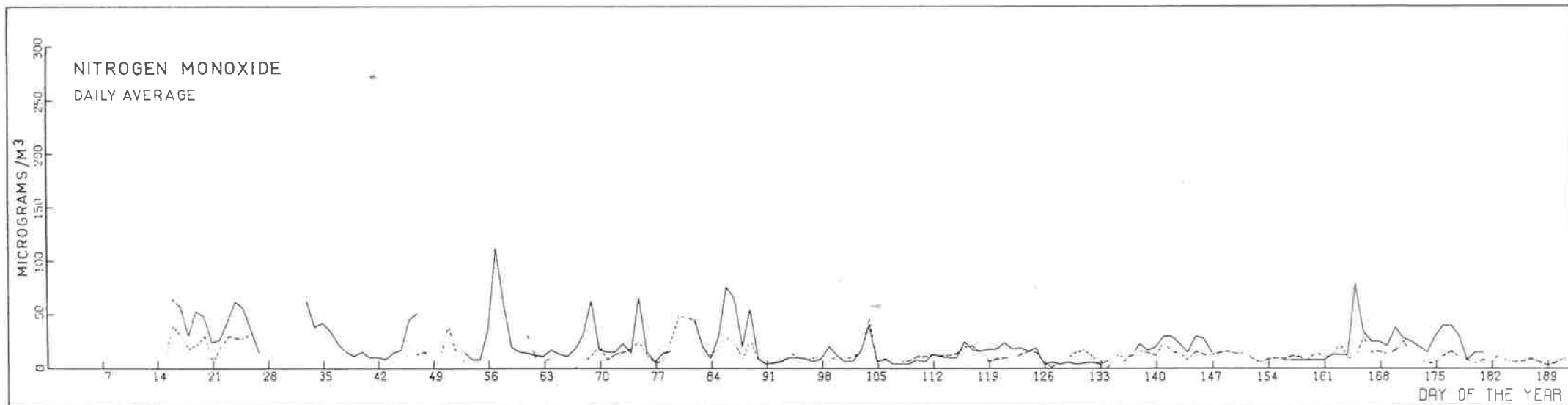
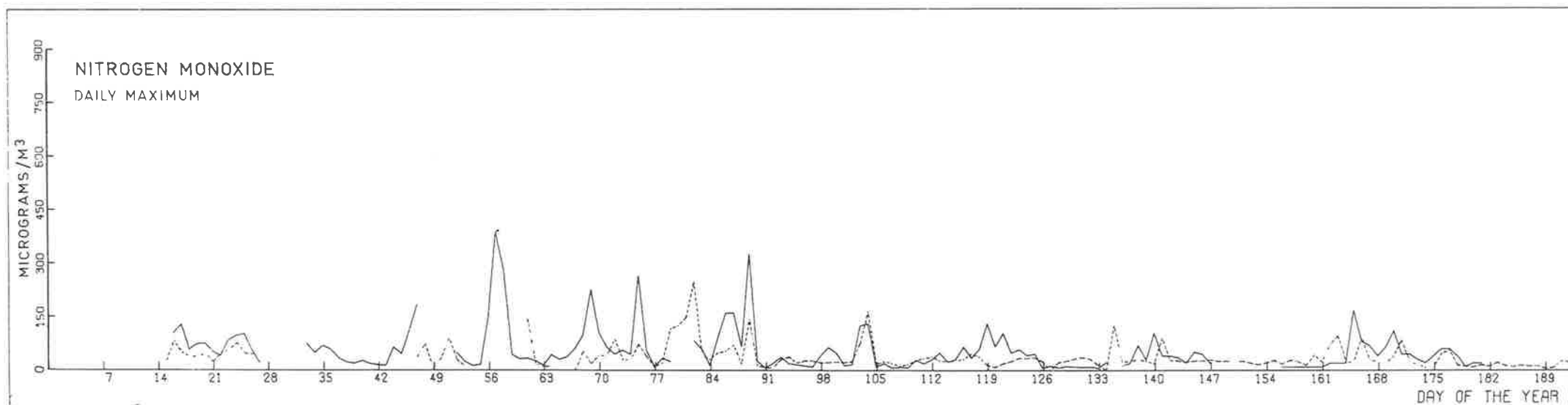


FIG. D 4. THE *daily maximum* CONCENTRATION OF *nitrogen monoxide*
IN VLAARDINGEN AND OMMOORD (IN MICROGRAMS/M³).



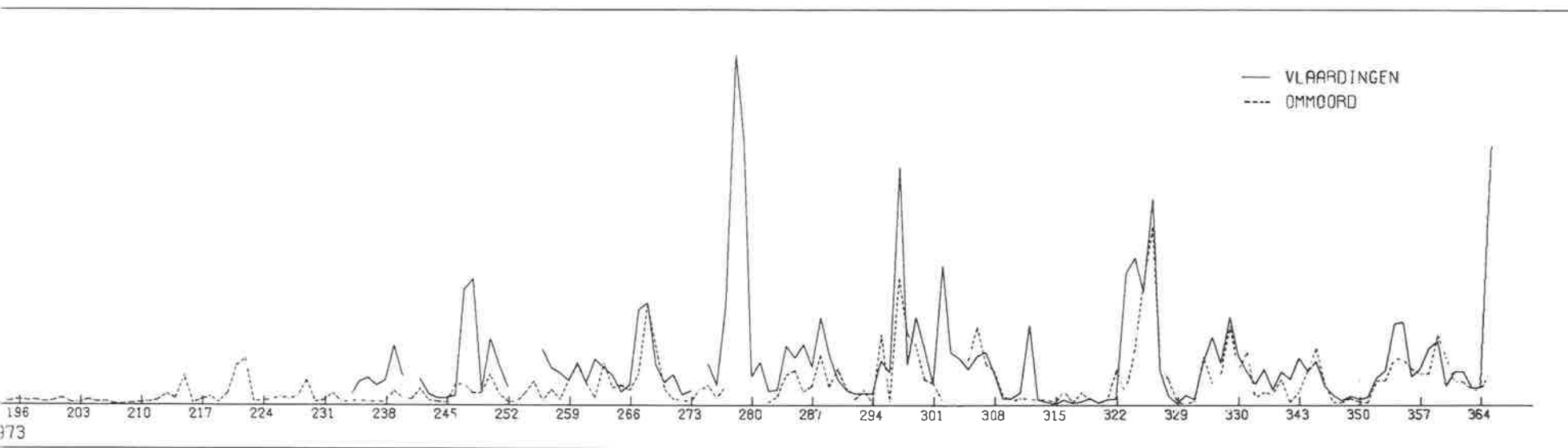
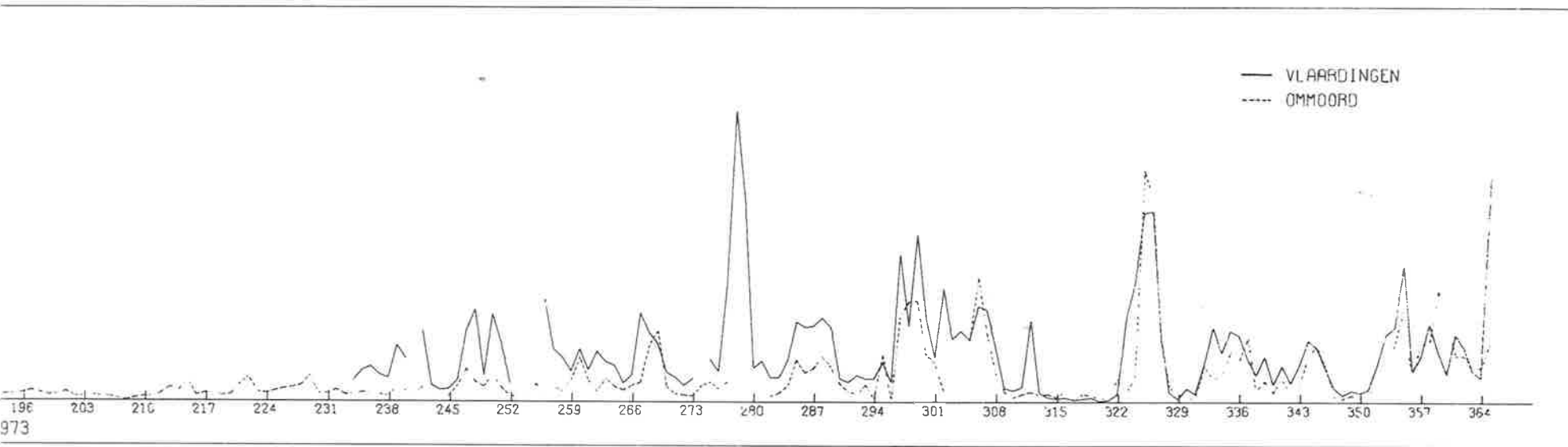


FIG. D 7. THE *daily average* CONCENTRATION OF *ozone* IN VLAARDINGEN
AND OMMOORD (IN MICROGRAMS/M³).

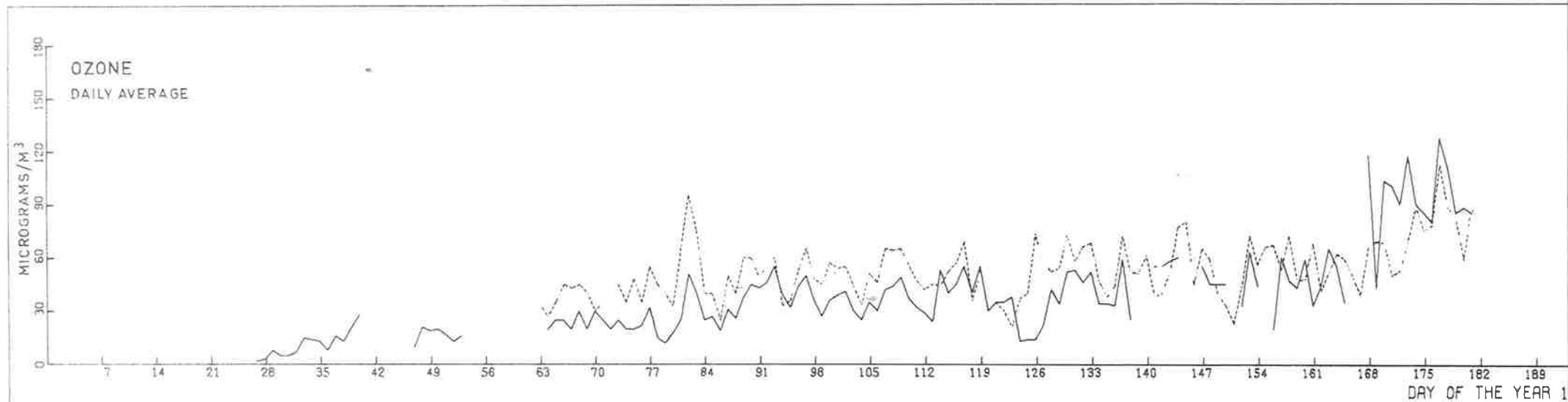
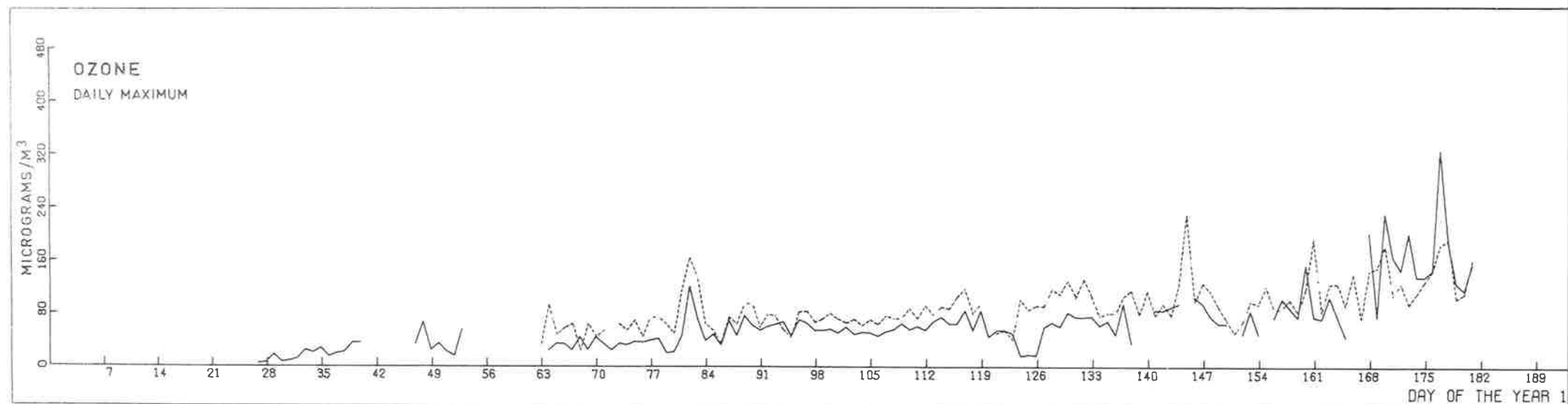


FIG. D 8. THE *daily maximum* CONCENTRATION OF *ozone* IN VLAARDINGEN
AND OMMOORD (IN MICROGRAMS/M³).



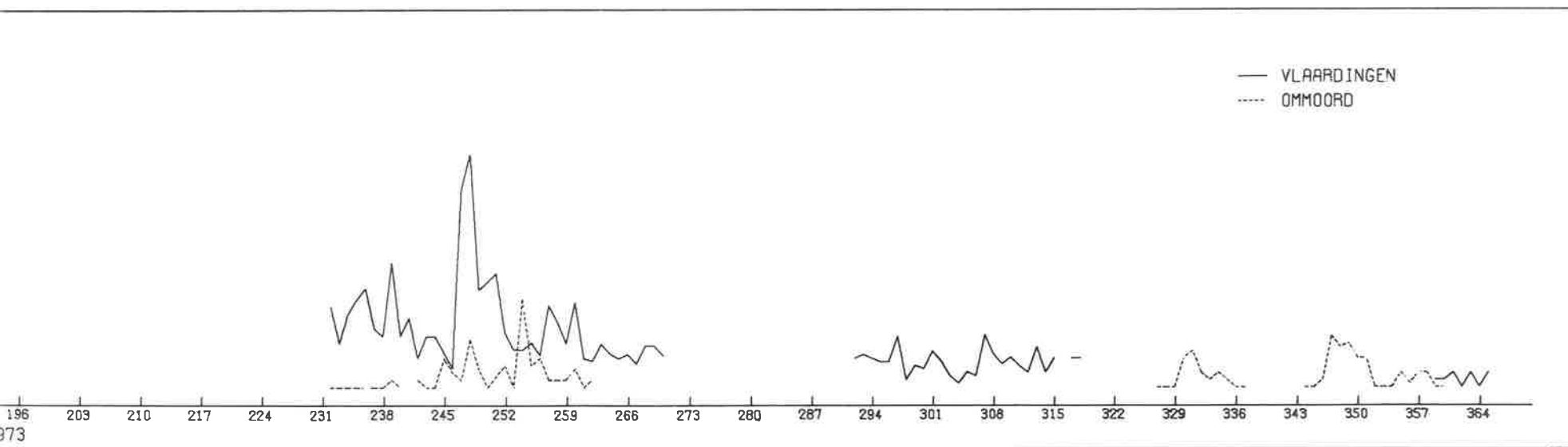
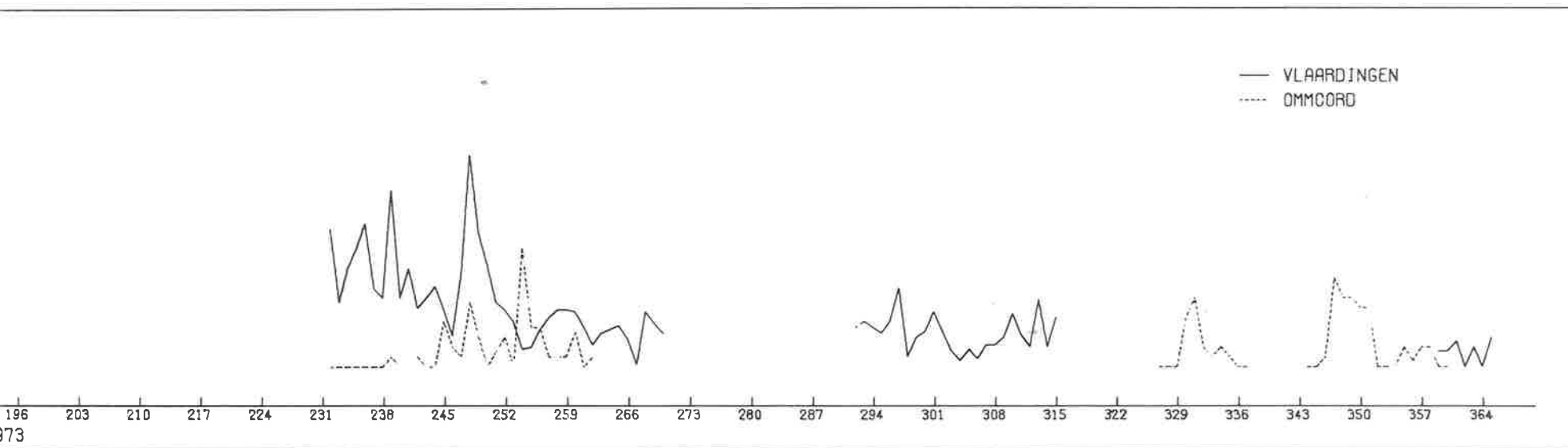


FIG. D 9. THE 24-hour average CONCENTRATION OF aldehydes IN
VLAARDINGEN AND OMMOORD (IN MICROGRAMS/M³).

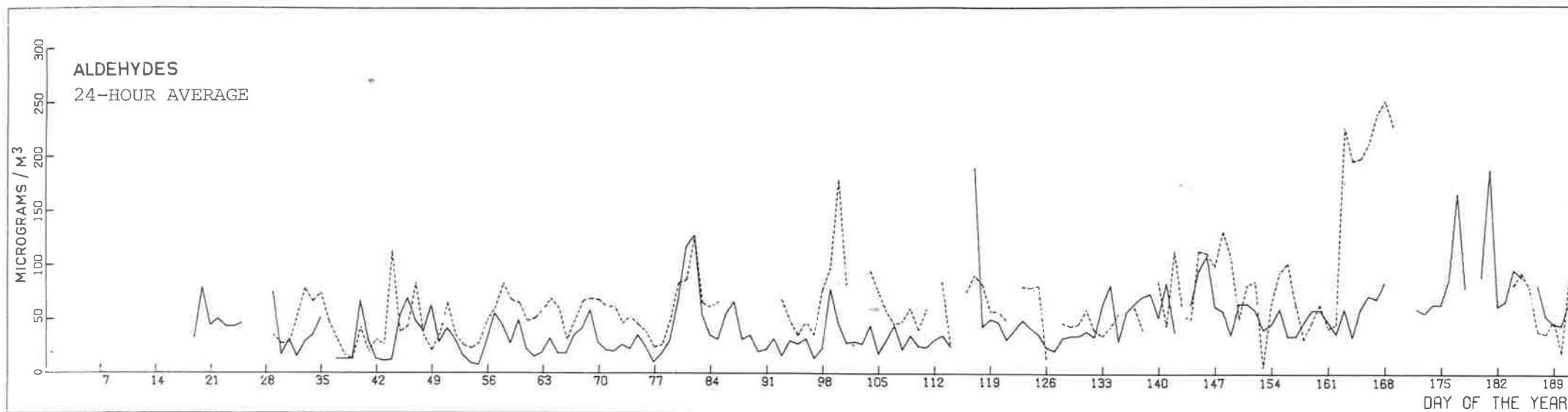
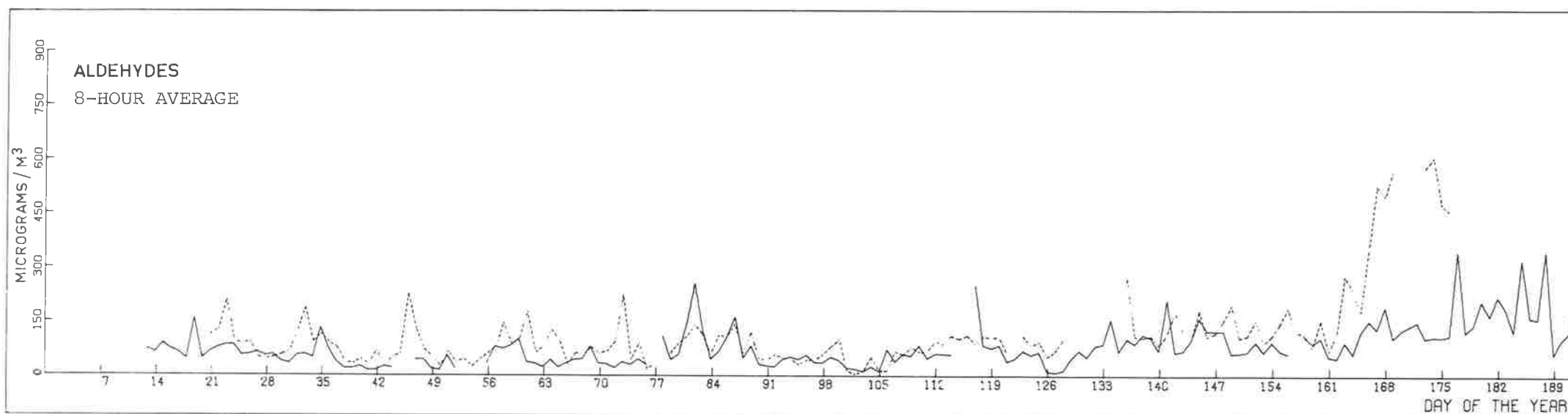
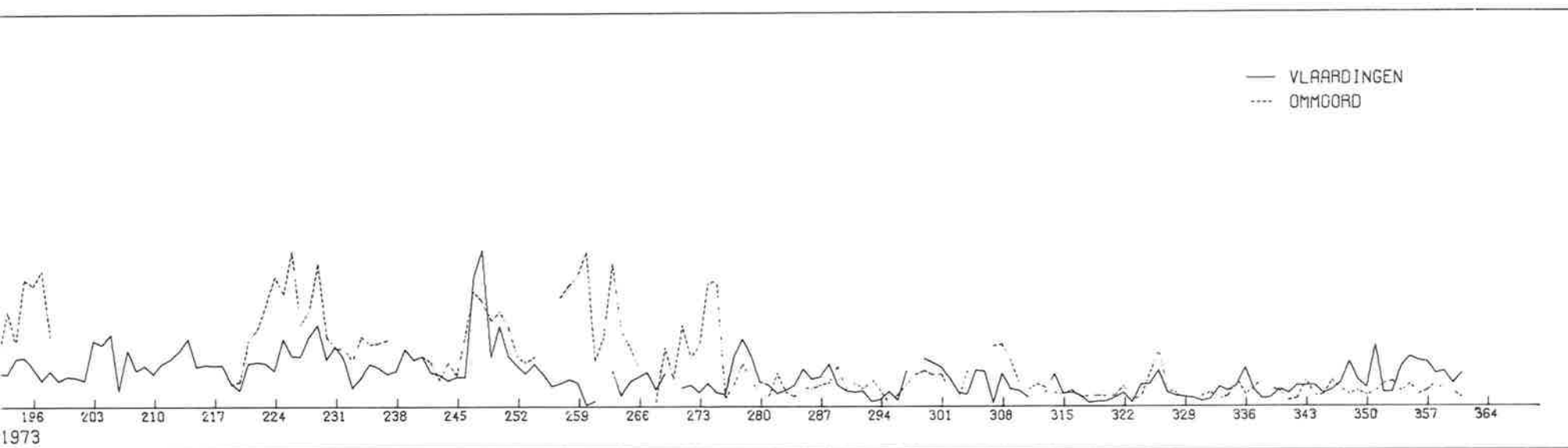
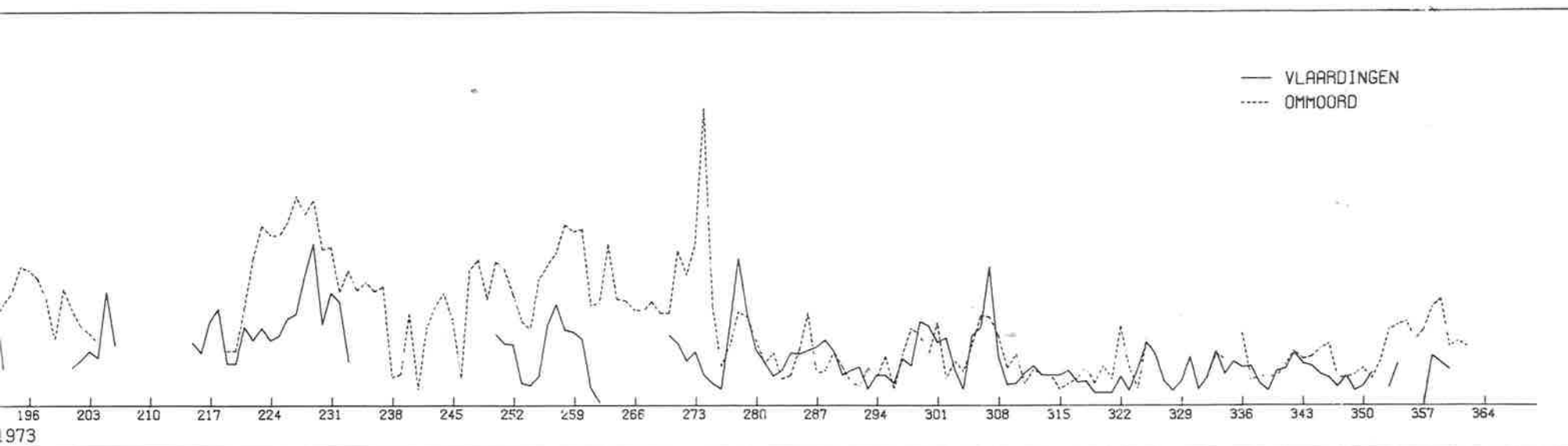


FIG. D 10. THE 8-hour average CONCENTRATION OF aldehydes IN
VLAARDINGEN AND OMMOORD (IN MICROGRAMS/M³).





APPENDIX E

FIGURES E 1 TO 4 SHOWING THE TEMPERATURE AND RELATIVE HUMIDITY
IN VLAARDINGEN AND OMMOORD DURING THE YEAR OF INVESTIGATION.

FIG. E 1. THE *maximum temperature* IN VLAARDINGEN AND OMMOORD
DURING THE YEAR OF INVESTIGATION (IN CENTIGRADES).

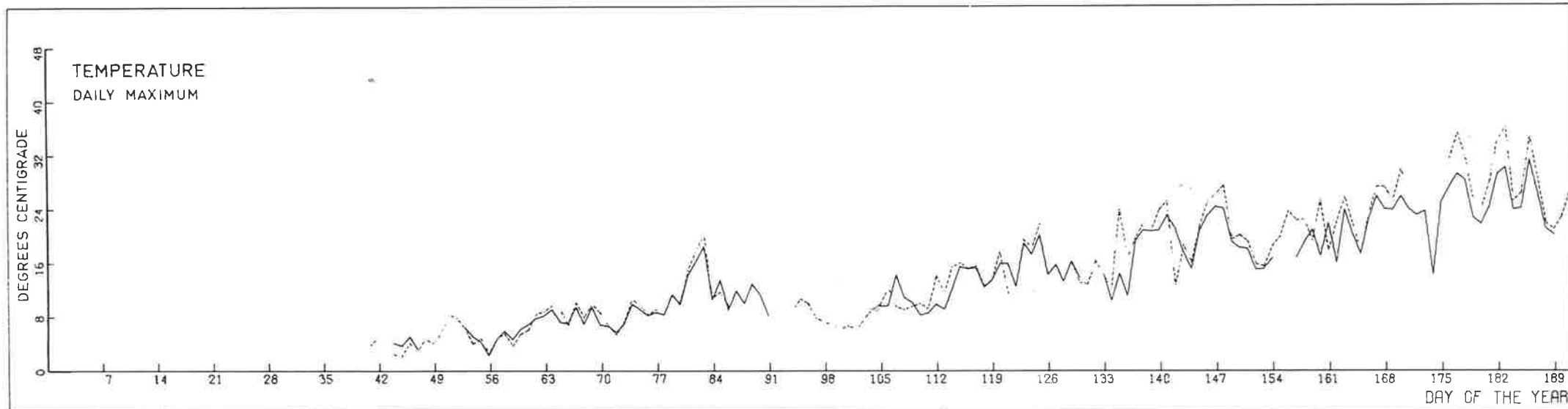
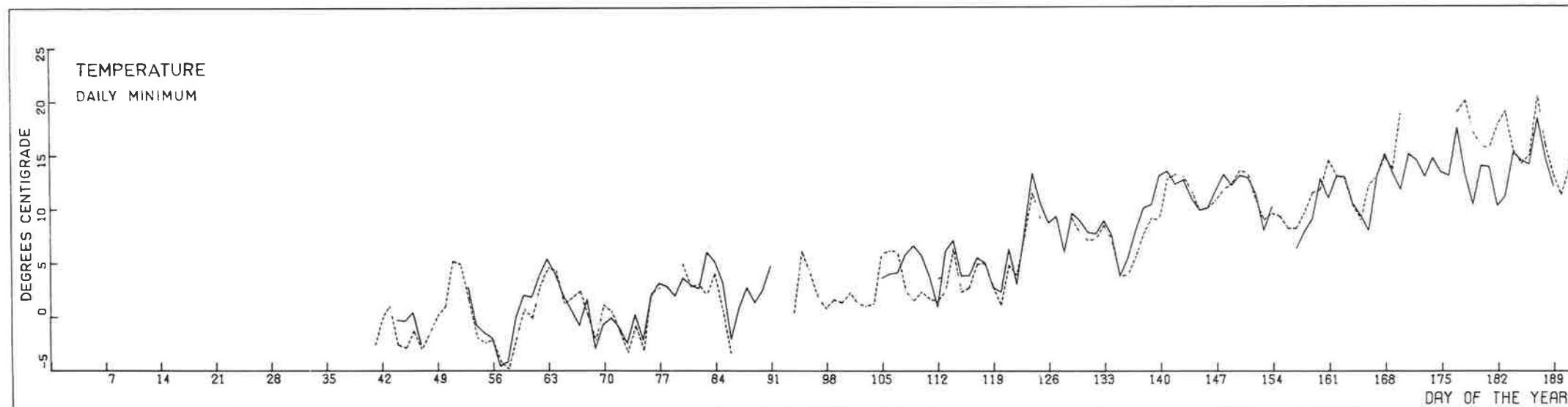


FIG. E 2. THE *minimum temperature* IN VLAARDINGEN AND OMMOORD
DURING THE YEAR OF INVESTIGATION (IN CENTIGRADES).



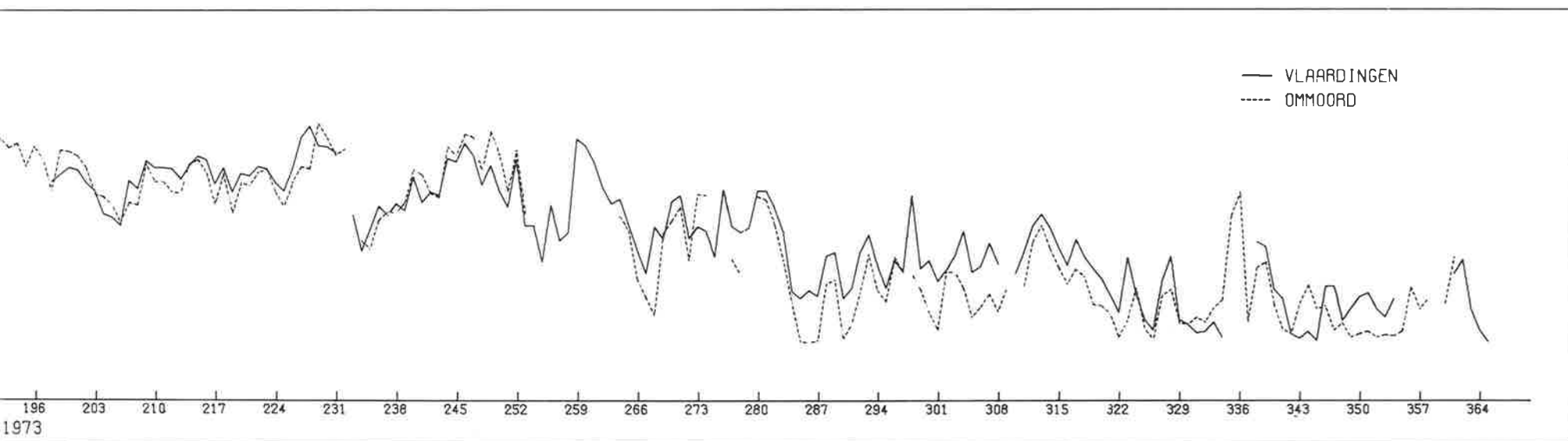
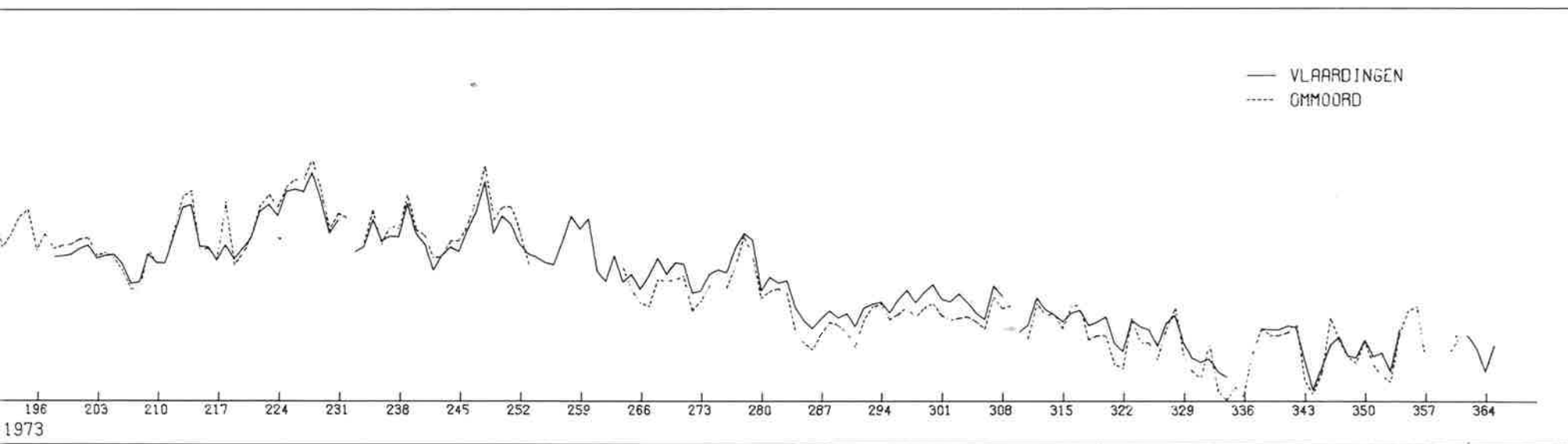


FIG. E. 3. THE *maximum relative humidity* IN VLAARDINGEN AND OMMOORD DURING THE YEAR OF INVESTIGATION (AS PERCENTAGE).

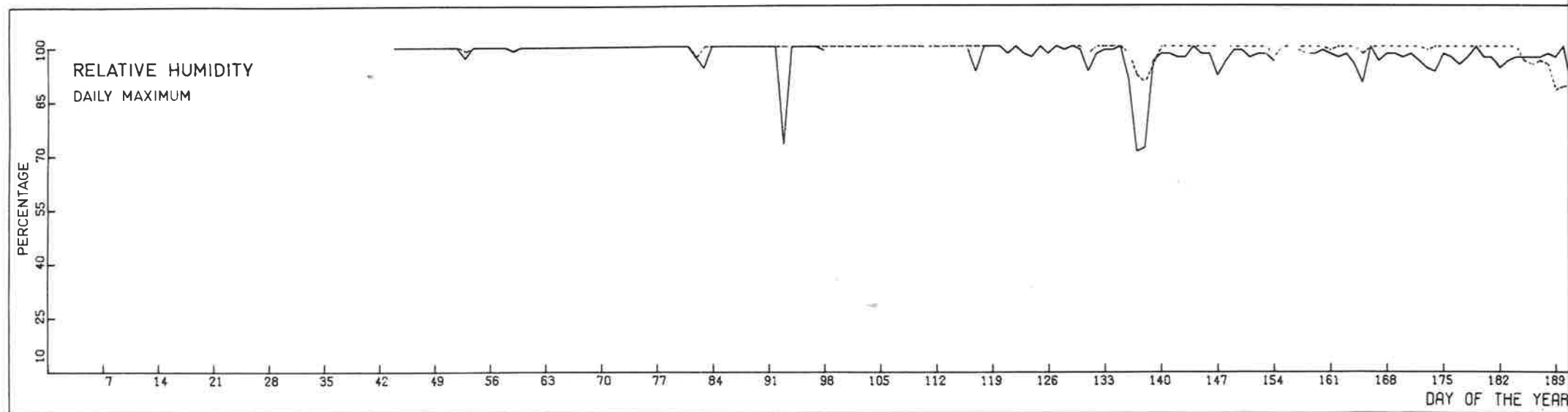
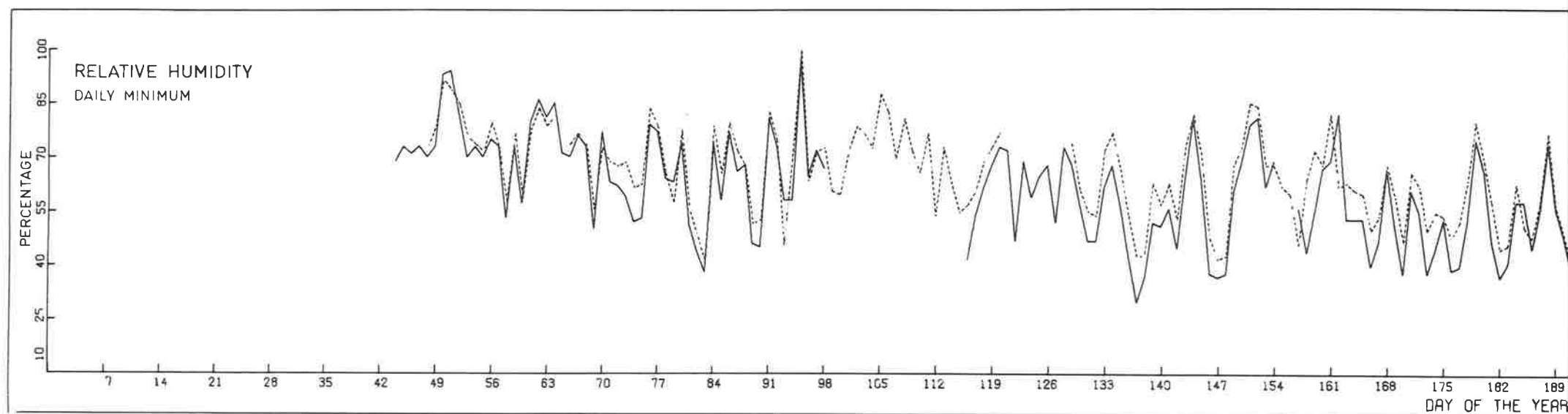
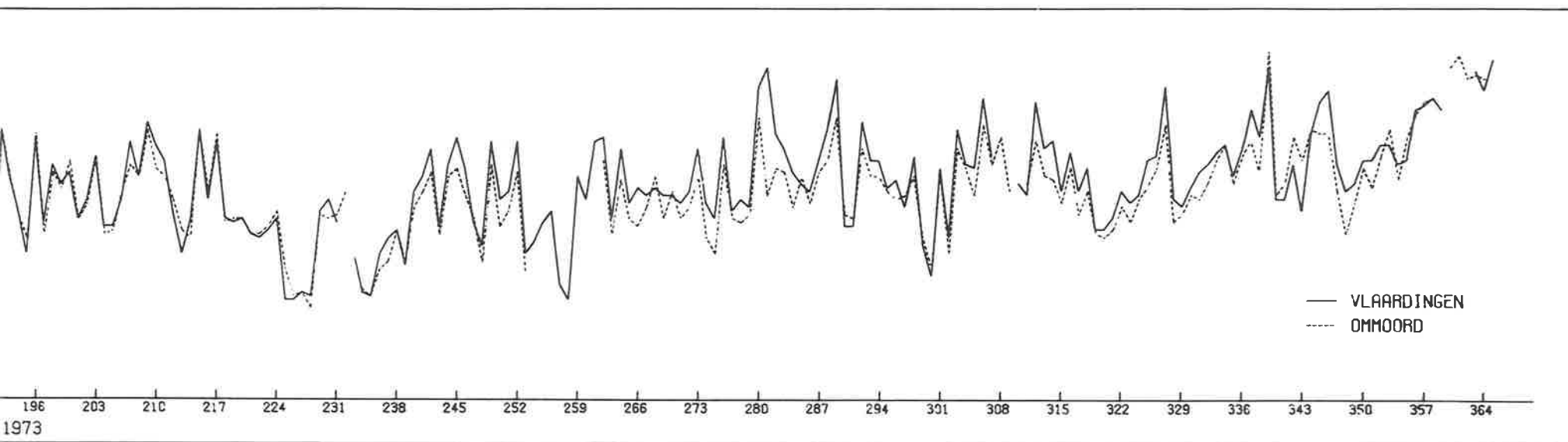
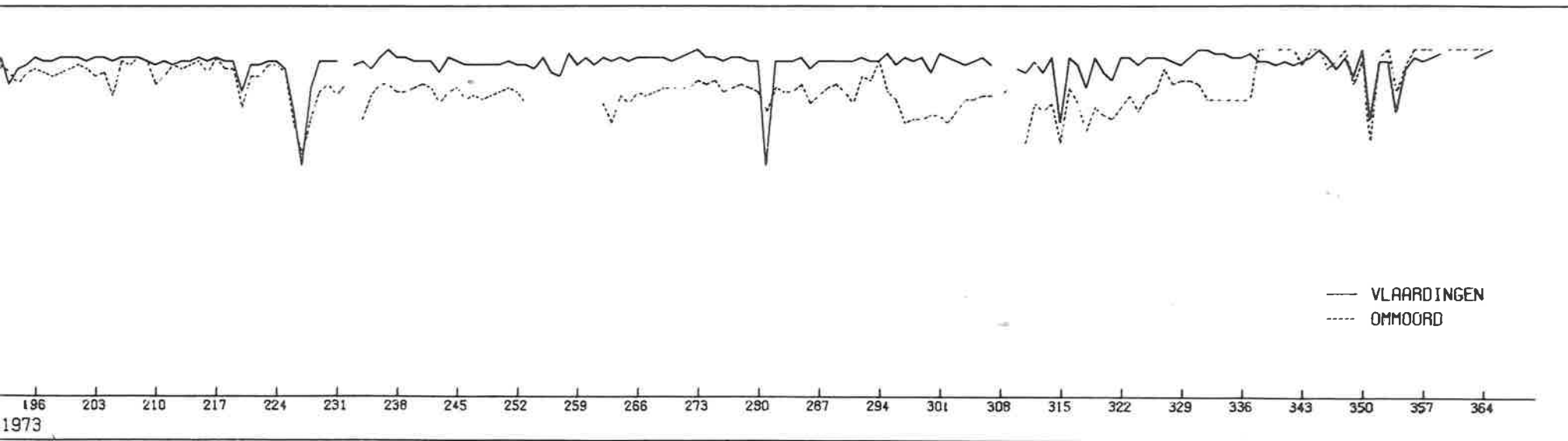


FIG. E 4. THE *minimum relative humidity* IN VLAARDINGEN AND OMMOORD DURING THE YEAR OF INVESTIGATION (AS PERCENTAGE).





TABLES

SHOWING THE ACTUAL VALUES PLOTTED IN THE GRAPHS IN THE
APPENDICES C, D, AND E.

TABLE C-1.1. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *cough* IN THE GROUP CNSLD grade 0.
(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	4	1.250	54:	122	0.221	109:	115	0.078	160:	103	0.097	211:	60	0.063	262:	104	-0.058
8:	23	0.174	55:	123	0.203	110:	116	-0.069	161:	104	0.096	212:	60	0.017	263:	104	-0.057
9:	38	0.211	56:	124	0.137	111:	115	-0.035	162:	103	0.126	213:	59	0.034	264:	103	-0.029
10:	59	0.119	57:	125	0.128	112:	115	0.009	163:	102	0.127	214:	59	0.034	265:	103	0.010
11:	71	0	58:	123	0.008	113:	116	-0.034	164:	102	0.049	215:	61	0.049	266:	104	0.067
12:	84	0.107	59:	122	-0.016	114:	117	-0.043	165:	102	0.049	216:	58	-0.052	267:	103	0.058
13:	87	0.034	60:	122	0.074	115:	117	0.060	166:	102	0.127	217:	62	0.015	268:	104	0.202
14:	89	0.135	61:	121	0.116	116:	116	0.034	167:	97	0.093	218:	64	0.047	269:	105	0.162
15:	94	-0.032	62:	119	0.185	117:	115	0.052	168:	97	0.144	219:	62	0.015	270:	105	0.161
16:	97	0.227	63:	120	0.167	118:	114	0.123	169:	97	0.175	220:	65	0.031	271:	103	0.165
17:	100	0.140	64:	120	0.133	119:	115	-0.034	170:	94	0.160	221:	65	0.077	272:	102	0.116
18:	103	0.087	65:	120	0.158	120:	117	-0.034	171:	91	0.253	222:	66	0.121	273:	104	0.154
19:	105	0.010	66:	123	0.130	121:	118	-0.093	172:	89	0.169	223:	66	0.152	274:	107	0.121
20:	106	-0.019	67:	123	-0.008	122:	118	-0.076	173:	85	0.259	224:	84	0.071	275:	107	0.103
21:	109	-0.018	68:	123	0.081	123:	117	-0.137	174:	85	0.153	225:	86	0.035	276:	106	0.066
22:	109	-0.037	69:	123	0.057	124:	117	-0.094	175:	80	0.262	226:	86	0.070	277:	107	0.159
23:	109	-0.009	70:	123	0.089	125:	116	0	176:	69	0.145	227:	86	0.081	278:	105	0.257
24:	110	0.009	71:	123	0.065	126:	117	-0.017	177:	63	0.111	228:	86	0.174	279:	105	0.200
25:	114	0.053	72:	123	0.098	127:	117	0.017	178:	57	0.088	229:	86	0.174	280:	104	0.221
26:	115	0.017	73:	120	0.058	128:	117	-0.034	179:	44	0.341	230:	86	0.140	281:	104	0.327
27:	115	0	74:	120	0.025	129:	117	0.017	180:	38	0.237	231:	92	0.064	282:	104	0.327
28:	119	0.025	75:	120	0.050	130:	114	0.026	181:	38	0.105	232:	95	0.053	283:	105	0.229
29:	118	0.025	76:	122	0.180	131:	113	0.044	182:	66	0.061	233:	97	0.165	284:	104	0.192
30:	119	0.134	77:	120	0.033	132:	113	0.027	183:	63	0.063	234:	98	0.112	285:	104	0.212
31:	122	0.074	78:	120	0.058	133:	112	0.125	184:	63	0.016	235:	97	0.072	286:	101	0.178
32:	122	0.041	79:	120	-0.017	134:	113	0.071	185:	62	-0.032	236:	96	-0.073	287:	102	0.167
33:	123	0.163	80:	118	0.212	135:	113	-0.009	186:	62	0	237:	96	-0.115	288:	102	0.196
34:	123	0.260	81:	117	0.205	136:	113	0.035	187:	62	-0.081	238:	102	-0.137	289:	103	0.117
35:	121	0.364	82:	118	0.085	137:	113	0.097	188:	63	-0.063	239:	99	0	290:	103	0.184
36:	123	0.309	83:	117	0.068	138:	113	0.097	189:	58	-0.052	240:	101	-0.059	291:	101	0.119
37:	124	0.331	84:	113	0.159	139:	112	0.125	190:	57	-0.035	241:	101	-0.010	292:	100	0.110
38:	124	0.226	85:	112	0.152	140:	112	0.054	191:	57	-0.018	242:	100	0.070	293:	102	0.118
39:	124	0.355	86:	111	0.099	141:	111	0.108	192:	55	-0.091	243:	98	0.061	294:	105	0.143
40:	124	0.274	87:	119	0	142:	111	0.054	193:	55	-0.073	244:	97	-0.031	295:	105	0.219
41:	124	0.218	88:	120	0.008	143:	111	0.108	194:	55	-0.091	245:	100	0.010	296:	104	0.231
42:	125	0.255	89:	121	0.025	144:	111	0.126	195:	53	-0.094	246:	100	0.090	297:	105	0.257
43:	124	0.177	90:	122	0.139	145:	111	0.009	196:	52	0.038	247:	100	0.020	298:	105	0.219
44:	124	0.113	91:	122	0.074	146:	110	0.036	197:	53	0.075	248:	99	0.091	299:	105	0.295
45:	125	0.112	92:	121	0.074	147:	110	0.045	198:	55	0.073	249:	99	0.162	300:	103	0.117
46:	125	0.112	93:	121	-0.025	148:	109	0.138	199:	56	0.107	250:	99	0.131	301:	104	0.144
47:	126	0.127	94:	121	0.025	149:	109	0.055	200:	56	0.107	251:	100	0.080	302:	103	-0.029
48:	126	-0.087	95:	121	0.008	150:	108	0.028	201:	54	0.019	252:	104	0.058	303:	104	-0.067
49:	126	-0.032	96:	120	0.058	151:	106	-0.078	202:	51	0.020	253:	105	-0.019	304:	103	0.184
50:	125	-0.048	97:	121	-0.017	152:	105	0.048	203:	52	0.154	254:	107	0.037	305:	103	0.165
51:	124	-0.089	98:	121	0.074	153:	105	-0.038	204:	53	0.113	255:	107	0.009	306:	102	0.078
52:	124	0.113	99:	121	0.124	154:	105	0.010	205:	52	0.115	256:	107	0.112	307:	100	0.100
53:	124	0.048	100:	120	0.075	155:	105	-0.029	206:	52	0.096	257:	105	0	308:	103	0.214
54:	124	-0.032	101:	118	-0.085	156:	106	0.009	207:	52	0.077	258:	105	-0.029	309:	103	0.136
55:	123	0.081	102:	117	-0.120	157:	104	0.087	208:	50	0	259:	105	0.038	310:	103	0.214
56:	125	0.072	103:	117	0.017	158:	104	0.048	209:	50	0	260:	105	-0.105	311:	102	0.186
57:	123	0.163	104:	116	0.103	159:	104	0.135	210:	61	0	261:	103	-0.056	312:	102	0.216
															313:	102	0.206
															314:	100	0.240
															315:	102	0.137
															316:	103	0.049
															317:	103	0.087
															318:	102	0.010
															319:	102	0.118
															320:	102	0.088
															321:	102	0.108
															322:	102	0.088
															323:	103	0
															324:	102	0.059
															325:	102	0.010
															326:	102	0.059
															327:	102	0.078
															328:	101	0.069
															329:	101	0.020
															330:	100	0.060
															331:	100	0.080
															332:	100	0.110
															333:	100	0.050
															334:	102	0.039
															335:	102	0.029
															336:	103	0.146
															337:	103	0.184
															338:	103	0.136
															339:	103	0.058
															340:	102	0.098
															341:	101	0.050
															342:	99	-0.061
															343:	101	-0.109
															344:	100	-0.030
															345:	100	0.050
															346:	99	0.051
															347:	99	-0.020
															348:	98	-0.061
															349:	98	0.020
															350:	99	0.081
															351:	63	-0.048
															352:	65	0
															353:	47	0.170
															354:	50	0.233
															355:	14	-0.053
															356:	12	-0.417
															357:	8	0.250
															358:	7	0.714

TABLE C-1.2. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *cough* IN THE GROUP *CNSLD grade 1*
(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	1	4.000	54:	108	0.352	109:	101	0.089	160:	89	0.169	211:	84	0.109	262:	99	0.253	313:	93	0.312	
8:	4	1.222	55:	109	0.422	110:	101	0.188	161:	90	0.256	212:	85	0.154	263:	90	0.240	314:	91	0.275	
9:	23	0.348	56:	109	0.450	111:	102	0.196	162:	90	0.267	213:	85	0.206	264:	97	0.412	315:	95	0.189	
10:	41	0.317	57:	109	0.404	112:	101	0.109	163:	89	0.213	214:	85	0.238	265:	97	0.351	316:	94	0.351	
11:	59	0.441	58:	109	0.413	113:	101	0.069	164:	90	0.256	215:	84	0.172	266:	94	0.500	317:	94	0.223	
12:	77	0.494	59:	107	0.523	114:	103	0.135	165:	90	0.267	216:	81	0.148	267:	95	0.274	318:	94	0.213	
13:	74	0.316	60:	106	0.443	115:	103	0.058	166:	89	0.213	217:	71	0.211	268:	96	0.240	319:	94	0.277	
14:	81	0.481	61:	107	0.477	116:	103	0.155	167:	88	0.227	218:	74	0.189	269:	96	0.282	320:	93	0.294	
15:	81	0.407	62:	107	0.393	117:	104	0.250	168:	90	0.233	219:	75	0.147	270:	98	0.205	321:	94	0.255	
16:	87	0.264	63:	107	0.374	118:	103	0.194	169:	90	0.256	220:	75	0.147	271:	97	0.340	322:	94	0.128	
17:	87	0.460	64:	107	0.340	119:	105	0.226	170:	90	0.300	221:	73	0.274	272:	94	0.479	323:	94	0.255	
18:	89	0.159	65:	107	0.243	120:	105	0.160	171:	88	0.330	222:	75	0.160	273:	93	0.269	324:	94	0.255	
19:	93	0.086	66:	107	0.065	121:	106	0.160	172:	86	0.326	223:	76	0.164	274:	96	0.229	325:	94	0.287	
20:	94	0.202	67:	107	0.159	122:	105	0.132	173:	85	0.482	224:	93	0.163	275:	96	0.104	326:	94	0.362	
21:	94	0.277	68:	106	0.315	123:	105	0.105	174:	82	0.524	225:	93	0.247	276:	97	0.134	327:	96	0.359	
22:	95	0.221	69:	105	0.139	124:	105	0.133	175:	73	0.438	226:	93	0.333	277:	97	0.113	328:	92	0.326	
23:	95	0.583	70:	107	0.159	125:	105	0.142	176:	67	0.339	227:	92	0.360	278:	97	0.258	329:	92	0.267	
24:	97	0.509	71:	107	0.047	126:	105	0.109	177:	55	0.400	228:	93	0.378	279:	96	0.417	330:	96	0.163	
25:	99	0.535	72:	107	0.093	127:	106	0.123	178:	45	0.400	229:	92	0.360	280:	95	0.505	331:	92	0.239	
26:	101	0.594	73:	107	0.093	128:	106	0.189	179:	41	0.317	230:	92	0.348	281:	95	0.388	332:	92	0.253	
27:	101	0.545	74:	108	0.040	129:	106	0.028	180:	33	0.091	231:	94	0.415	282:	95	0.358	333:	91	0.341	
28:	102	0.382	75:	108	-0.037	130:	105	-0.019	181:	31	0.032	232:	94	0.330	283:	95	0.211	334:	93	0.361	
29:	101	0.355	76:	106	0.194	131:	105	-0.029	182:	54	0.241	233:	94	0.234	284:	95	0.174	335:	95	0.290	
30:	101	0.168	81:	109	0.147	132:	105	-0.047	183:	54	0.370	234:	92	0.239	285:	94	0.138	336:	95	0.194	
31:	102	0.373	82:	109	0.303	133:	107	0.065	184:	53	0.434	235:	93	0.359	286:	89	0.292	337:	93	0.075	
32:	102	0.500	83:	109	0.257	134:	107	0.084	185:	53	0.113	236:	92	0.272	287:	88	0.250	338:	93	0.097	
33:	102	0.304	84:	108	-0.056	135:	107	0.158	186:	53	0.075	237:	91	0.297	288:	88	0.239	339:	93	0.151	
34:	102	0.304	85:	108	0.056	136:	105	0.198	187:	52	-0.135	238:	94	0.296	289:	88	0.375	340:	93	0.151	
35:	105	0.434	86:	107	-0.009	137:	105	0.181	188:	52	-0.173	239:	94	0.234	290:	89	0.404	341:	93	0.183	
36:	105	0.267	87:	106	0.028	138:	103	0.292	189:	55	-0.236	240:	94	0.372	291:	88	0.341	342:	93	0.140	
37:	105	0.264	88:	105	0.105	139:	104	0.135	190:	56	-0.125	241:	94	0.436	292:	88	0.455	343:	94	0.340	
38:	105	0.195	89:	105	0.152	140:	103	0.135	191:	55	-0.055	242:	93	0.280	293:	88	0.273	344:	94	0.234	
39:	107	0.215	90:	105	0.143	141:	105	0.286	192:	55	-0.036	243:	91	0.352	294:	93	0.312	345:	94	0.160	
40:	107	0.294	91:	104	0.166	142:	104	0.260	193:	55	-0.055	244:	90	0.335	295:	94	0.351	346:	92	0.163	
41:	107	0.421	92:	105	0.162	143:	103	0.311	194:	54	-0.259	245:	92	0.467	296:	94	0.362	347:	91	0.176	
42:	107	0.402	93:	108	0.194	144:	102	0.333	195:	51	-0.255	246:	92	0.522	297:	93	0.355	348:	90	0.267	
43:	107	0.271	94:	108	0.222	145:	101	0.396	196:	48	-0.083	247:	93	0.419	298:	93	0.430	349:	90	0.278	
44:	107	0.318	95:	108	0.241	146:	99	0.374	197:	47	0.064	248:	94	0.445	299:	93	0.430	350:	91	0.253	
45:	107	0.306	96:	106	0.066	147:	97	0.209	198:	47	0.149	249:	95	0.442	300:	92	0.467	351:	95	0.200	
46:	107	0.187	97:	106	0.113	148:	97	0.371	199:	47	0	250:	94	0.466	301:	95	0.347	352:	87	0.194	
47:	106	0.396	98:	105	0.057	149:	96	0.312	200:	46	0.109	251:	94	0.394	302:	95	0.311	353:	96	-0.083	
48:	105	0.352	99:	105	0.105	150:	97	0.351	201:	47	0	252:	95	0.506	303:	95	0.337	354:	91	-0.032	
49:	105	0.352	100:	104	0.077	151:	94	0.479	202:	42	-0.095	253:	96	0.466	304:	94	0.346	355:	95	0.067	
50:	105	0.438	101:	104	0.048	152:	93	0.430	203:	41	0.220	254:	97	0.423	305:	93	0.387	356:	93	0.308	
51:	105	0.462	102:	102	0.039	153:	92	0.424	204:	41	0.098	255:	97	0.445	306:	93	0.286	357:	8	0	
52:	105	0.509	103:	103	0.107	154:	95	0.296	205:	40	0.300	256:	97	0.526	307:	92	0.359	358:	8	0	
53:	108	0.394	104:	103	0.255	155:	95	0.333	206:	40	0.375	257:	97	0.495	308:	93	0.323	359:	8	0	
54:	108	0.444	105:	104	0.038	156:	96	0.333	207:	41	0.366	258:	97	0.464	309:	93	0.140	360:	6	0	
55:	108	0.339	106:	104	0.029	157:	94	0.415	208:	42	0.119	259:	100	0.500	310:	93	0.226	361:	6	0	
56:	108	0.339	107:	104	-0.119	158:	93	0.183	209:	43	0.233	260:	100	0.360	311:	93	0.226	362:	2	0	
57:	108	0.324	108:	102	0.049	159:	91	0.209	210:	63	0.095	261:	99	0.313	312:	93	0.312	363:	1	0	

TABLE C-1.3. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *cough* IN THE GROUP *CNSLD grade 2+3*
(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	3	0	94:	94	0.138	109:	91	-0.473	140:	90	-0.267	211:	95	-0.232	262:	83	-0.145
8:	17	-1.133	95:	94	-0.021	110:	91	-0.484	141:	90	-0.200	212:	94	-0.111	263:	83	-0.072
9:	25	-0.885	96:	94	0.090	111:	91	-0.451	142:	90	-0.256	213:	99	-0.130	264:	82	-0.103
10:	42	-0.571	97:	93	0	112:	91	-0.352	143:	89	-0.292	214:	90	-0.007	265:	83	-0.252
11:	55	-0.792	98:	94	0.053	113:	90	-0.318	144:	88	-0.250	215:	60	0.017	266:	80	-0.209
12:	65	-0.785	99:	95	0.021	114:	93	-0.372	145:	87	-0.184	216:	97	-0.193	267:	85	-0.271
13:	68	-0.750	100:	95	-0.021	115:	92	-0.283	146:	88	-0.103	217:	92	-0.274	268:	84	-0.247
14:	75	-0.615	101:	95	-0.155	116:	95	-0.147	147:	88	-0.125	218:	65	-0.075	269:	84	-0.190
15:	74	-0.662	102:	98	-0.153	117:	93	-0.172	148:	89	-0.090	219:	67	-0.149	270:	85	-0.353
16:	74	-0.554	103:	98	-0.173	118:	93	-0.344	149:	89	-0.045	220:	66	-0.091	271:	81	-0.370
17:	75	-0.621	104:	98	-0.020	119:	95	-0.242	150:	90	0.022	221:	66	-0.152	272:	77	-0.208
18:	76	-0.657	105:	98	-0.102	120:	95	-0.147	151:	90	-0.033	222:	69	-0.110	273:	81	-0.172
19:	85	-0.588	106:	97	0.072	121:	95	-0.116	152:	87	0.011	223:	68	-0.200	274:	97	-0.088
20:	85	-0.430	107:	97	0.072	122:	94	-0.095	153:	87	0.057	224:	85	-0.235	275:	88	-0.210
21:	87	-0.374	108:	96	0.083	123:	94	-0.117	154:	85	0.047	225:	87	-0.120	276:	87	-0.287
22:	88	-0.466	109:	97	0.021	124:	94	-0.043	155:	76	0.026	226:	87	0	277:	88	-0.284
23:	89	-0.545	110:	97	0.031	125:	92	-0.033	156:	65	0.169	227:	86	0.050	278:	80	-0.395
24:	91	-0.390	111:	97	0.100	126:	92	-0.109	157:	62	0.226	228:	85	0.100	279:	87	-0.333
25:	92	-0.348	112:	97	0.010	127:	93	0.032	158:	52	0.192	229:	83	0.024	280:	86	-0.372
26:	92	-0.435	113:	97	0.010	128:	93	0.129	159:	45	0.289	230:	83	-0.064	281:	87	-0.230
27:	92	-0.413	114:	97	0.155	129:	92	0.141	160:	32	0.125	231:	90	0.011	282:	86	-0.302
28:	93	-0.366	115:	95	-0.021	130:	92	0.261	161:	31	0.065	232:	91	0.044	283:	85	-0.200
29:	94	-0.447	116:	95	0.084	131:	91	0.198	162:	53	-0.302	233:	90	0.055	284:	85	-0.424
30:	95	-0.242	117:	95	0.147	132:	92	0.272	163:	52	-0.288	234:	89	0	285:	83	-0.337
31:	97	-0.185	118:	95	0.147	133:	91	0.285	164:	51	-0.157	235:	89	-0.011	286:	81	-0.346
32:	95	-0.281	119:	94	-0.064	134:	92	0.183	165:	51	-0.157	236:	89	-0.022	287:	82	-0.256
33:	97	-0.144	120:	94	-0.043	135:	92	0.141	166:	50	-0.180	237:	80	-0.093	288:	81	-0.259
34:	97	-0.062	121:	93	-0.204	136:	90	0.144	167:	47	-0.213	238:	85	0	289:	81	-0.198
35:	97	-0.093	122:	94	-0.160	137:	90	0.133	168:	44	-0.159	239:	82	-0.130	290:	79	-0.152
36:	97	0.041	123:	92	-0.087	138:	88	0.170	169:	49	-0.082	240:	82	-0.037	291:	81	-0.210
37:	95	-0.062	124:	91	-0.033	139:	89	0.090	170:	49	-0.102	241:	82	-0.024	292:	82	-0.341
38:	95	-0.042	125:	90	-0.044	140:	93	0.011	171:	49	-0.102	242:	81	-0.025	293:	81	-0.358
39:	95	-0.187	126:	87	-0.241	141:	93	0.011	172:	50	-0.160	243:	80	0.012	294:	87	-0.009
40:	95	-0.145	127:	91	-0.110	142:	94	0.053	173:	50	-0.240	244:	78	0.020	295:	86	-0.110
41:	96	-0.219	128:	95	-0.084	143:	94	0.064	174:	48	-0.104	245:	80	0.150	296:	86	-0.244
42:	96	-0.240	129:	96	-0.052	144:	94	-0.021	175:	43	-0.256	246:	81	0.074	297:	85	-0.221
43:	96	-0.177	130:	96	-0.104	145:	95	0.032	176:	45	-0.089	247:	81	0.198	298:	86	-0.151
44:	98	-0.214	131:	96	-0.156	146:	93	-0.022	177:	43	-0.279	248:	81	0.140	299:	87	-0.230
45:	98	-0.275	132:	95	-0.200	147:	92	0.011	178:	43	-0.279	249:	82	0.110	300:	87	-0.172
46:	99	-0.192	133:	95	-0.232	148:	92	0.043	179:	43	-0.279	250:	82	0.037	301:	88	-0.057
47:	99	-0.182	134:	95	-0.229	149:	91	0.165	180:	42	-0.310	251:	81	0.025	302:	88	-0.102
48:	99	-0.242	135:	96	-0.094	150:	91	0.077	181:	41	-0.171	252:	84	0	303:	88	-0.193
49:	99	-0.071	136:	96	-0.150	151:	92	0.087	182:	39	-0.615	253:	85	-0.105	304:	88	-0.125
50:	96	-0.094	137:	95	-0.305	152:	91	0.055	183:	42	-0.405	254:	84	0	305:	88	-0.080
51:	97	-0.113	138:	95	-0.187	153:	91	0.022	184:	40	-0.425	255:	83	-0.161	306:	85	-0.141
52:	97	-0.103	139:	95	-0.350	154:	94	-0.202	185:	40	-0.550	256:	84	-0.155	307:	84	-0.080
53:	97	-0.103	140:	94	-0.394	155:	93	-0.140	186:	40	-0.450	257:	85	-0.224	308:	85	0.094
54:	97	-0.093	141:	94	-0.363	156:	91	-0.253	187:	42	-0.381	258:	84	-0.143	309:	86	-0.081
55:	97	-0.103	142:	93	-0.367	157:	91	-0.286	188:	42	-0.310	259:	85	-0.094	310:	86	-0.035
56:	95	-0.211	143:	93	-0.419	158:	91	-0.297	189:	42	-0.357	260:	84	-0.107	311:	85	-0.047
57:	95	-0.054	144:	91	-0.407	159:	91	-0.264	190:	52	-0.212	261:	83	-0.044	312:	85	-0.044
															313:	84	-0.190
															314:	85	-0.254
															315:	84	-0.298
															316:	84	-0.310
															317:	84	-0.345
															318:	84	-0.190
															319:	84	-0.345
															320:	86	-0.256
															321:	87	-0.379
															322:	86	-0.442
															323:	85	-0.412
															324:	86	-0.570
															325:	85	-0.271
															326:	85	-0.224
															327:	85	-0.259
															328:	85	-0.282
															329:	86	-0.337
															330:	87	-0.230
															331:	86	-0.467
															332:	86	-0.337
															333:	84	-0.357
															334:	85	-0.235
															335:	85	-0.141
															336:	84	-0.030
															337:	84	-0.060
															338:	82	-0.037
															339:	83	0.036
															340:	83	-0.060
															341:	83	0.072
															342:	82	0.163
															343:	84	-0.048
															344:	84	-0.036
															345:	83	-0.060
															346:	81	-0.037
															347:	83	-0.036
															348:	83	-0.145
															349:	82	-0.171
															350:	80	-0.212
															351:	88	-0.162
															352:	77	-0.263
															353:	45	-0.467
															354:	32	-0.219
															355:	21	0.238
															356:	15	0.400
															357:	11	0.091
															358:	11	0.091
															359:	10	0.200
															360:	10	0.400

TABLE C-2.1. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *phlegm* IN THE GROUP *CNSLD grade 0*

(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	4	0	54:	123	-0.010	109:	115	0.043	160:	103	0.029	211:	60	0.150	262:	104	0	313:	102	-0.029
8:	23	-0.261	55:	123	0.010	110:	115	-0.026	161:	104	0.038	212:	60	0.083	263:	104	-0.067	314:	100	-0.040
9:	34	-0.079	56:	124	0.105	111:	115	-0.009	162:	103	0.049	213:	59	0.102	264:	103	-0.068	315:	103	0
10:	54	0.068	57:	125	0.010	112:	116	-0.017	163:	102	0.039	214:	59	0.085	265:	103	-0.029	316:	103	0.010
11:	71	-0.014	58:	123	0.138	113:	115	-0.034	164:	102	0.020	215:	61	0.164	266:	105	-0.038	317:	103	0.049
12:	82	0.111	59:	122	0.041	114:	117	-0.051	165:	102	0.010	216:	58	0.009	267:	103	-0.039	318:	102	0.069
13:	95	-0.035	60:	122	0.074	115:	117	-0.034	166:	102	0.029	217:	62	0	268:	104	-0.010	319:	102	0.069
14:	89	0	61:	121	0.008	116:	116	-0.078	167:	97	0.072	218:	64	0	269:	105	-0.029	320:	102	0.029
15:	94	-0.085	62:	119	0	117:	115	-0.104	168:	97	0.062	219:	65	0	270:	105	-0.038	321:	102	0.049
16:	97	0.010	63:	120	0.033	118:	114	-0.035	169:	97	0.082	220:	65	0.015	271:	103	0.019	322:	102	0.059
17:	94	-0.010	64:	120	0.067	119:	115	-0.059	170:	94	0.032	221:	65	0.077	272:	102	0.020	323:	101	0.040
18:	103	0.058	65:	120	0.008	120:	116	-0.076	171:	91	0.055	222:	66	0.061	273:	104	-0.025	324:	102	0.010
19:	105	-0.038	66:	123	0.065	121:	118	-0.008	172:	89	0.045	223:	66	0.106	274:	107	-0.047	325:	102	0.010
20:	105	-0.009	67:	123	0.033	122:	118	-0.008	173:	85	0.082	224:	84	0.063	275:	107	-0.047	326:	102	0.010
21:	107	-0.064	68:	123	0.049	123:	117	-0.068	174:	85	0.059	225:	85	0.093	276:	106	-0.019	327:	102	0
22:	104	0.018	69:	123	-0.008	124:	117	-0.034	175:	85	0.075	226:	85	0.093	277:	107	0.037	328:	101	-0.040
23:	109	-0.055	70:	123	-0.033	125:	116	-0.009	176:	69	-0.029	227:	86	0.093	278:	105	0.010	329:	100	0.010
24:	110	-0.027	71:	123	-0.057	126:	117	-0.017	177:	63	0.063	228:	86	0.128	279:	105	0.010	330:	99	-0.071
25:	114	-0.018	72:	123	-0.033	127:	117	0.060	178:	57	0.018	229:	86	0.128	280:	105	0.019	331:	99	0.030
26:	114	-0.070	73:	120	-0.075	128:	117	0.077	179:	44	0.091	230:	85	0.128	281:	105	0.019	332:	99	0.051
27:	114	-0.061	74:	123	-0.042	129:	115	0.052	180:	38	0.053	231:	95	0.084	282:	105	0.019	333:	99	0.030
28:	119	-0.017	75:	120	-0.350	130:	115	0.017	181:	38	0.053	232:	95	0	283:	106	-0.019	334:	101	0.050
29:	115	-0.093	76:	122	-0.074	131:	113	-0.027	182:	55	0.077	233:	97	-0.031	284:	105	0.057	335:	101	0.069
30:	119	-0.050	77:	120	-0.042	132:	113	0	183:	63	0.063	234:	98	-0.092	285:	105	0.105	336:	103	0
31:	122	-0.015	78:	123	-0.008	133:	112	-0.009	184:	63	0.063	235:	97	-0.041	286:	102	0.069	337:	103	0.029
32:	122	-0.107	79:	120	-0.008	134:	113	0	185:	62	0.081	236:	95	-0.052	287:	103	0.049	338:	103	0.068
33:	123	-0.073	80:	118	0.042	135:	113	-0.009	186:	62	0.065	237:	96	-0.062	288:	103	0.058	339:	103	0.058
34:	123	-0.089	81:	117	0.026	136:	113	0	187:	62	0.065	238:	101	-0.050	289:	103	0.014	340:	102	0.078
35:	122	-0.090	82:	118	0.025	137:	113	0.053	188:	63	0.048	239:	100	0	290:	103	0.029	341:	101	0.050
36:	123	-0.057	83:	117	0.009	138:	113	0.009	189:	58	0.069	240:	101	-0.030	291:	101	0.010	342:	99	-0.081
37:	124	0.040	84:	113	0.018	139:	112	0.018	190:	57	0.070	241:	101	-0.010	292:	100	-0.020	343:	101	-0.051
38:	124	0.073	85:	112	-0.027	140:	112	0	191:	57	0.035	242:	100	0.030	293:	102	0.010	344:	100	-0.070
39:	124	0.040	86:	111	0.036	141:	111	0	192:	55	0.055	243:	98	0.041	294:	105	0.067	345:	100	-0.040
40:	124	0.016	87:	119	-0.025	142:	111	0	193:	55	0.055	244:	97	0.031	295:	104	0.067	346:	99	0
41:	124	0.097	88:	120	-0.033	143:	111	0.027	194:	55	0.055	245:	100	0.030	296:	104	0.096	347:	99	0.051
42:	120	0.056	89:	121	0	144:	111	-0.004	195:	53	0.057	246:	100	0	297:	105	0.029	348:	98	0.041
43:	124	0.024	90:	122	0	145:	111	-0.027	196:	52	0.115	247:	100	0	298:	105	0.029	349:	96	-0.010
44:	124	0.048	91:	121	0.017	146:	110	-0.009	197:	53	0.075	248:	99	0	299:	105	0.086	350:	99	0.020
45:	120	0.032	92:	121	-0.025	147:	110	0.009	198:	55	0.091	249:	99	0	300:	103	0.066	351:	83	-0.312
46:	125	0.080	93:	121	-0.050	148:	109	-0.018	199:	56	0.071	250:	99	0.030	301:	104	0.058	352:	84	-0.031
47:	125	-0.024	94:	120	-0.017	149:	109	0	200:	56	0.089	251:	100	0.030	302:	103	0.058	353:	47	-0.043
48:	126	-0.040	95:	120	0.025	150:	107	0.047	201:	54	0.074	252:	104	0.036	303:	104	0.010	354:	24	0.034
49:	126	-0.050	100:	121	0.041	151:	106	0	202:	51	0.078	253:	105	0.067	304:	103	0.107	355:	14	0.053
50:	129	-0.088	101:	121	0.025	152:	105	0.029	203:	52	0.077	254:	107	0.065	305:	103	0.047	356:	12	-0.250
51:	124	-0.153	102:	121	0.008	153:	105	0.029	204:	53	0.151	255:	107	0.037	306:	102	0	357:	8	0
52:	124	-0.145	103:	121	0.033	154:	104	0.048	205:	52	0.115	256:	107	0.037	307:	100	0.050	358:	7	0
53:	124	-0.065	104:	120	0.058	155:	104	0.048	206:	52	0.096	257:	105	-0.010	308:	103	0.014	359:	6	0
54:	124	-0.032	105:	118	-0.075	156:	105	0.010	207:	52	0.096	258:	105	-0.010	309:	103	-0.014	360:	6	0
55:	123	0.033	106:	117	-0.043	157:	103	0.068	208:	50	0.100	259:	105	0	310:	103	-0.014	361:	5	0
56:	129	0.032	107:	117	0.026	158:	103	0.068	209:	50	0.140	260:	105	0.024	311:	102	-0.010	362:	3	0
57:	123	-0.033	108:	116	0.086	159:	104	0.029	210:	61	0.148	261:	103	0.049	312:	102	-0.010	363:	1	0

(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

[illegible]

(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	3	0	98:	94	0.117	109:	91	-0.165	160:	90	-0.133	211:	89	-0.162	262:	83	-0.145
8:	12	-1.057	99:	94	0.149	110:	91	-0.198	161:	90	-0.167	212:	84	0	263:	83	-0.072
9:	20	-0.423	100:	94	0.074	111:	91	-0.319	162:	90	0.089	213:	89	-0.091	264:	83	-0.120
10:	42	-0.341	101:	93	-0.064	112:	91	-0.121	163:	89	-0.067	214:	60	0.090	265:	83	-0.159
11:	33	-0.623	102:	94	-0.117	113:	90	-0.178	164:	88	0	215:	60	0.007	266:	86	-0.174
12:	62	-0.589	103:	95	-0.063	114:	93	-0.097	165:	87	-0.069	216:	67	-0.035	267:	89	-0.294
13:	56	-0.670	104:	95	-0.211	115:	93	-0.194	166:	87	0.011	217:	62	-0.194	268:	85	-0.153
14:	70	-0.448	105:	97	-0.247	116:	94	-0.223	167:	88	-0.034	218:	60	-0.161	269:	84	-0.167
15:	74	-0.270	106:	98	-0.214	117:	92	-0.141	168:	89	-0.079	219:	57	-0.164	270:	85	-0.141
16:	74	-0.041	107:	97	-0.224	118:	92	-0.196	169:	89	-0.034	220:	55	-0.030	271:	81	-0.309
17:	71	-0.410	108:	97	-0.135	119:	95	-0.032	170:	90	-0.022	221:	67	-0.134	272:	77	-0.312
18:	78	-0.423	109:	98	-0.031	120:	95	0.053	171:	90	-0.022	222:	69	-0.067	273:	67	-0.195
19:	85	-0.459	110:	97	-0.092	121:	95	-0.063	172:	87	0.023	223:	68	-0.261	274:	91	-0.121
20:	85	-0.353	111:	97	0.072	122:	94	-0.043	173:	87	0.023	224:	69	-0.193	275:	88	-0.057
21:	87	-0.235	112:	96	0.119	123:	94	-0.032	174:	86	0	225:	67	-0.023	276:	87	-0.115
22:	88	-0.193	113:	97	0.010	124:	94	-0.021	175:	75	0.026	226:	65	0	277:	86	-0.114
23:	85	-0.264	114:	97	0.031	125:	91	0.033	176:	65	-0.046	227:	65	-0.109	278:	67	-0.115
24:	91	-0.352	115:	97	0.052	126:	91	-0.011	177:	62	-0.068	228:	65	-0.071	279:	67	-0.126
25:	92	-0.239	116:	97	0.093	127:	93	-0.043	178:	62	-0.231	229:	83	-0.012	280:	86	-0.209
26:	92	-0.272	117:	97	-0.010	128:	93	0.094	179:	45	0.156	230:	83	-0.285	281:	66	-0.198
27:	92	-0.293	118:	97	-0.052	129:	92	0.076	180:	32	0	231:	90	-0.044	282:	66	-0.314
28:	93	-0.290	119:	95	-0.125	130:	92	0.130	181:	31	0.032	232:	91	0.088	283:	69	-0.271
29:	94	-0.713	120:	95	-0.189	131:	91	0.132	182:	53	-0.170	233:	90	-0.011	284:	85	-0.694
30:	95	-0.621	121:	95	-0.011	132:	92	0.033	183:	52	-0.096	234:	88	-0.034	285:	83	0.012
31:	97	-0.124	122:	95	-0.189	133:	91	-0.143	184:	51	-0.216	235:	89	-0.011	286:	80	-0.152
32:	96	-0.052	123:	94	-0.109	134:	92	0.065	185:	51	-0.098	236:	89	0.045	287:	82	-0.232
33:	97	-0.610	124:	94	-0.043	135:	92	0.087	186:	50	-0.140	237:	85	-0.047	288:	81	-0.025
34:	97	-0.010	125:	93	0.011	136:	90	0.133	187:	47	0	238:	85	-0.059	289:	81	-0.037
35:	97	0.041	126:	94	-0.011	137:	90	0.078	188:	44	-0.023	239:	82	-0.195	290:	79	-0.051
36:	97	-0.010	127:	92	-0.070	138:	85	0.045	189:	49	-0.020	240:	82	0.073	291:	81	-0.113
37:	95	-0.159	128:	90	-0.111	139:	91	-0.067	190:	49	-0.020	241:	82	0.024	292:	82	-0.159
38:	96	0.021	129:	89	-0.101	140:	93	0	191:	49	0.061	242:	81	0.062	293:	81	-0.062
39:	95	-0.167	130:	87	-0.057	141:	93	0	192:	50	-0.060	243:	80	0.157	294:	87	0
40:	95	0.031	131:	93	-0.122	142:	94	-0.011	193:	50	-0.180	244:	78	0.103	295:	86	-0.023
41:	95	-0.177	132:	94	0.021	143:	94	-0.021	194:	48	-0.043	245:	80	0.012	296:	86	-0.070
42:	95	-0.167	133:	95	0.021	144:	94	-0.032	195:	43	-0.116	246:	81	0.123	297:	86	-0.038
43:	95	-0.115	134:	95	-0.116	145:	95	-0.042	196:	45	0.133	247:	81	0.163	298:	87	0.034
44:	95	-0.122	135:	95	-0.147	146:	95	-0.097	197:	43	0.093	248:	81	0.140	299:	87	-0.092
45:	97	-0.103	136:	94	-0.117	147:	92	-0.043	198:	43	-0.372	249:	82	0.244	300:	87	0.057
46:	94	-0.040	137:	95	-0.221	148:	92	0.075	199:	43	-0.349	250:	82	0.317	301:	88	0.011
47:	94	-0.152	138:	95	-0.109	149:	91	0.187	200:	42	-0.286	251:	81	0.222	302:	88	0.034
48:	94	-0.124	139:	95	0.031	150:	91	0.011	201:	41	-0.268	252:	84	0.167	303:	88	-0.034
49:	94	-0.051	140:	95	-0.229	151:	92	-0.069	202:	38	-0.316	253:	85	0.062	304:	88	-0.097
50:	95	-0.073	141:	95	-0.157	152:	91	-0.132	203:	41	-0.293	254:	84	0.174	305:	88	0
51:	97	-0.155	142:	96	-0.063	153:	91	-0.066	204:	39	-0.205	255:	83	-0.024	306:	86	0
52:	97	-0.124	143:	95	-0.289	154:	94	-0.128	205:	39	-0.179	256:	84	-0.036	307:	84	-0.095
53:	97	-0.144	144:	94	-0.249	155:	92	-0.011	206:	39	-0.179	257:	85	0	308:	85	0.054
54:	97	-0.227	145:	94	-0.064	156:	91	0.011	207:	41	-0.122	258:	84	-0.167	309:	86	-0.140
55:	97	-0.113	146:	93	-0.161	157:	91	-0.033	208:	41	-0.073	259:	85	-0.212	310:	86	-0.035
56:	97	-0.179	147:	93	-0.219	158:	91	-0.171	209:	41	-0.341	260:	84	-0.131	311:	89	-0.129
57:	95	-0.011	148:	91	-0.242	159:	91	-0.187	210:	51	-0.333	261:	83	-0.045	312:	85	-0.212

189

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	4	0	98:	123	0.0057	109:	119	-0.0052	160:	103	0.0019	211:	59	0.1000	262:	104	0
8:	23	0.130	98:	123	0.0024	110:	116	-0.0052	161:	104	0.0029	212:	60	0.1000	263:	104	0.0077
9:	38	0.184	98:	124	-0.0008	111:	119	-0.0017	162:	103	0.0019	213:	59	0.1002	264:	103	0
10:	59	0.102	98:	125	0.0024	112:	116	-0.0017	163:	102	0.0020	214:	59	0.1002	265:	103	0
11:	71	-0.0014	98:	123	0.0057	113:	116	-0.0017	164:	102	-0.0020	215:	61	0.0008	266:	105	0
12:	82	0.0073	98:	122	-0.0057	114:	117	-0.0091	165:	102	-0.0020	216:	59	0.0034	267:	103	-0.0039
13:	95	0.0039	98:	122	-0.0057	115:	117	-0.0017	166:	102	0.0029	217:	62	0.0032	268:	104	-0.0010
14:	89	0.135	98:	121	-0.0041	116:	115	0.0017	167:	97	0.0031	218:	64	0.0031	269:	105	-0.0038
15:	94	0.0089	98:	119	-0.0039	117:	115	-0.0009	168:	97	0.0031	219:	65	0.0092	270:	105	0
16:	97	0.134	98:	120	-0.100	118:	114	-0.0044	169:	97	0.0041	220:	65	0.0031	271:	103	0.0058
17:	94	-0.0010	98:	120	-0.0042	119:	113	-0.0017	170:	94	0.0032	221:	65	0.0031	272:	102	0.0029
18:	103	0.0010	98:	120	-0.0042	120:	118	-0.0017	171:	91	0.0033	222:	65	0.0030	273:	104	0.0029
19:	100	-0.0085	98:	123	0	121:	118	-0.0091	172:	89	0.0067	223:	65	0.0091	274:	107	0.0065
20:	105	-0.0023	98:	122	0	122:	118	-0.0029	173:	85	0.0035	224:	64	0.119	275:	107	0.0028
21:	109	-0.0046	98:	123	0.0041	123:	117	-0.0026	174:	85	0.0035	225:	65	0.116	276:	106	0.0028
22:	105	-0.0037	98:	123	0	124:	117	0.0009	175:	80	0.112	226:	65	0.116	277:	107	0.0065
23:	109	0.0037	98:	123	0.0004	125:	115	0.0009	176:	69	0	227:	65	0.1174	278:	105	0.0068
24:	110	0.0035	98:	123	-0.0041	126:	117	0.0009	177:	63	0	228:	65	0.1174	279:	105	0.124
25:	114	0.0061	98:	123	-0.0008	127:	117	0.0009	178:	57	0	229:	65	0.116	280:	105	0.143
26:	119	0.0039	98:	120	0.0029	128:	117	0.0077	179:	44	0	230:	85	0.116	281:	105	0.190
27:	119	0	98:	120	0.0058	129:	117	0.0060	180:	38	0.0079	231:	95	-0.0021	282:	105	0.105
28:	115	-0.0034	98:	120	0.0058	130:	114	0.0053	181:	38	0.0079	232:	95	0.0021	283:	106	0.0028
29:	118	-0.0029	98:	122	0.123	131:	112	-0.0062	182:	65	0.0031	233:	97	0.0021	284:	105	0.0067
30:	119	0.0034	98:	120	0.0092	132:	113	-0.0062	183:	63	0.0032	234:	95	0.0061	285:	105	0.0067
31:	122	0.004	98:	120	0.0092	133:	112	-0.0027	184:	63	0.0032	235:	97	0.103	286:	102	0.0024
32:	122	0.0041	98:	120	0.0092	134:	113	-0.0062	185:	62	0.0032	236:	96	0.0021	287:	103	0.0078
33:	123	-0.0008	98:	118	0.127	135:	113	-0.0027	186:	62	0.0032	237:	96	-0.0021	288:	103	0.0068
34:	123	0.0016	98:	117	0.137	136:	113	-0.0018	187:	62	0.0032	238:	101	-0.0020	289:	103	0.0068
35:	122	0.0008	98:	116	0.162	137:	113	-0.0053	188:	63	0.0032	239:	100	-0.0020	290:	103	0.0068
36:	123	0.0033	98:	117	0.060	138:	113	-0.0027	189:	58	0.0034	240:	101	0.0020	291:	101	0.0069
37:	124	0.0059	98:	113	0.067	139:	112	-0.0062	190:	57	0.0035	241:	101	0.0020	292:	100	0.0030
38:	124	0.004	98:	112	0.067	140:	112	-0.0054	191:	57	0.0035	242:	100	0.0020	293:	101	0.0069
39:	124	0.121	98:	111	0.067	141:	111	-0.0054	192:	55	0.0036	243:	99	0.0020	294:	100	0.0067
40:	124	0.0059	98:	119	0.025	142:	111	-0.0054	193:	55	0.0036	244:	97	0.0021	295:	104	0.0029
41:	124	0.0053	98:	120	0.025	143:	111	-0.0018	194:	55	0.0036	245:	100	0.0020	296:	104	0.0057
42:	125	0.0032	98:	121	0.058	144:	111	-0.0054	195:	53	0.0038	246:	100	0.0020	297:	105	0.0029
43:	124	0.0059	98:	122	0.057	145:	111	-0.0054	196:	52	-0.0019	247:	100	0.0070	298:	105	0.0029
44:	124	0.0049	98:	121	0.025	146:	110	-0.0055	197:	53	-0.0019	248:	99	0.101	299:	105	0.0095
45:	125	0.0059	98:	121	0.025	147:	110	-0.0009	198:	55	-0.0018	249:	99	0.0091	300:	103	0.0097
46:	125	0.0088	98:	121	0.058	148:	109	-0.0009	199:	56	-0.0018	250:	99	0.0091	301:	104	0.0058
47:	125	0.0087	98:	121	0.025	149:	109	-0.0009	200:	56	0.0054	251:	100	0.0020	302:	103	0.0058
48:	125	0.0095	98:	121	0.083	150:	107	-0.0019	201:	54	0.0056	252:	104	0.0019	303:	104	0.0057
49:	125	0.0059	100:	121	-0.0017	151:	105	-0.0019	202:	51	0.0059	253:	105	0.0019	304:	103	0.0058
50:	125	0.0024	101:	121	0.0008	152:	105	-0.0019	203:	52	0.115	254:	107	0.0019	305:	103	0.0058
51:	124	-0.0008	102:	121	0.0008	153:	105	-0.0057	204:	53	0.113	255:	107	0.0019	306:	102	0.0059
52:	124	0.004	103:	121	-0.0029	154:	105	-0.0057	205:	52	0.115	256:	107	0.0019	307:	100	0.100
53:	124	0.0008	104:	120	-0.0058	155:	105	-0.0019	206:	52	0.115	257:	105	0.0019	308:	103	0.0058
54:	124	0	105:	117	0.0009	156:	106	-0.0019	207:	52	0.115	258:	105	0.0019	309:	103	0.0097
55:	123	0.0024	106:	117	-0.0026	157:	104	-0.0019	208:	50	0.200	259:	105	-0.0019	310:	103	0.0058
56:	123	0.0024	107:	117	-0.0000	158:	103	0.0019	209:	50	0.120	260:	105	-0.0019	311:	102	0.0068
57:	123	0.0024	108:	116	-0.0017	159:	104	0.0019	210:	61	0.098	261:	104	-0.0019	312:	102	0.0068

TABLE C-3.2. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *dyspnoea* IN THE GROUP *CNSLD grade 1*

(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	1	0	53:	106	0.028	109:	101	0.109	160:	99	0.079	211:	64	0.094	262:	99	0.192
8:	5	0.550	54:	109	0.073	110:	101	0.109	161:	90	0.078	212:	59	0.154	263:	90	0.104
9:	23	-0.522	55:	103	0.019	111:	102	0.078	162:	90	0.067	213:	63	0.098	264:	97	0.105
10:	41	0.073	56:	109	-0.037	112:	101	0.099	163:	89	0.067	214:	63	0.167	265:	97	0.062
11:	57	-0.051	57:	109	0.059	113:	101	0.128	164:	89	0.056	215:	54	0.109	266:	94	0.128
12:	77	0.075	58:	107	0.028	114:	103	0.148	165:	90	0.133	216:	61	0	267:	90	0.031
13:	74	-0.013	59:	106	0.089	115:	103	0.097	166:	89	0.180	217:	71	-0.014	268:	96	0.083
14:	41	0.123	60:	109	0.023	116:	103	0.117	167:	88	0.239	218:	74	0.095	269:	90	0.031
15:	81	0.148	61:	108	0.009	117:	104	0.125	168:	89	0.247	219:	75	-0.013	270:	98	-0.010
16:	87	0.149	62:	105	0	118:	103	0.146	169:	90	0.211	220:	75	-0.067	271:	97	0
17:	88	-0.091	63:	108	-0.038	119:	105	0.075	170:	90	0.178	221:	73	0.014	272:	94	0.021
18:	89	0.090	64:	105	-0.067	120:	106	0.104	171:	89	0.170	222:	75	-0.040	273:	91	-0.066
19:	93	-0.097	65:	105	-0.142	121:	106	0.113	172:	85	0.163	223:	75	-0.053	274:	95	0.021
20:	94	0.128	66:	110	0.060	122:	105	0.076	173:	85	0.106	224:	93	0.022	275:	90	0.031
21:	94	-0.043	67:	107	0.065	123:	104	0.173	174:	82	0.122	225:	93	0.032	276:	97	0
22:	95	-0.109	68:	107	0.121	124:	105	0.086	175:	73	0.192	226:	93	0.034	277:	97	-0.010
23:	95	-0.052	69:	105	0.151	125:	105	0.095	176:	62	0.113	227:	92	0.033	278:	97	0.093
24:	97	0.031	70:	105	0.019	126:	104	0.077	177:	55	0.127	228:	93	0.085	279:	90	0.125
25:	95	0.010	71:	105	0	127:	104	0.058	178:	45	0.133	229:	92	0.070	280:	94	0.106
26:	101	0	72:	106	0.028	128:	104	0.048	179:	41	0.195	230:	92	0.065	281:	95	0.084
27:	101	-0.168	73:	107	0.023	129:	105	0.057	180:	33	0.061	231:	94	0.043	282:	95	0.042
28:	102	-0.185	74:	107	0.093	130:	105	0.057	181:	31	0	232:	94	-0.032	283:	95	0.137
29:	101	0.010	75:	107	0.234	131:	106	0.085	182:	54	-0.093	233:	94	-0.043	284:	95	0.116
30:	101	-0.089	76:	108	0.185	132:	106	0.123	183:	54	-0.019	234:	92	-0.094	285:	93	0.054
31:	102	-0.010	77:	108	-0.028	133:	107	0.093	184:	53	-0.019	235:	93	-0.075	286:	89	-0.034
32:	102	0.078	78:	109	-0.130	134:	107	0.058	185:	53	-0.019	236:	92	0.043	287:	88	-0.057
33:	102	0.069	79:	107	-0.028	135:	107	-0.009	186:	53	0.057	237:	91	0	288:	88	-0.034
34:	102	-0.059	80:	107	-0.093	136:	106	0.104	187:	52	0.096	238:	94	-0.032	289:	88	-0.023
35:	105	-0.208	81:	105	-0.047	137:	105	0.067	188:	52	0.077	239:	94	0.033	290:	89	-0.076
36:	105	-0.109	82:	105	0.045	138:	102	0.088	189:	55	-0.036	240:	94	0.064	291:	88	-0.023
37:	105	-0.079	83:	104	0	139:	104	0.058	190:	56	0.018	241:	94	0.064	292:	88	0.034
38:	105	-0.038	84:	104	0.119	140:	103	0.039	191:	55	0.036	242:	93	0.075	293:	88	0.057
39:	107	0.079	85:	104	0.129	141:	105	0.057	192:	55	0.036	243:	90	0.122	294:	93	0
40:	107	0	86:	104	0.212	142:	104	0.058	193:	55	0.036	244:	90	0.059	295:	94	0.032
41:	107	0.047	87:	106	0.132	143:	103	0.029	194:	54	0.074	245:	93	0.191	296:	94	-0.011
42:	104	0.059	88:	107	0.168	144:	102	0.108	195:	51	-0.020	246:	93	0.200	297:	93	-0.086
43:	107	0.093	89:	108	0.102	145:	101	0.010	196:	48	0.062	247:	94	0.100	298:	93	0.054
44:	105	0.028	90:	108	0.102	146:	99	0.101	197:	47	0.064	248:	95	0.126	299:	93	-0.065
45:	107	0	91:	109	0.164	147:	97	0.072	198:	47	0.213	249:	90	0.198	300:	93	-0.054
46:	107	-0.112	92:	109	0.143	148:	97	0.041	199:	47	0.128	250:	95	0.110	301:	95	0.105
47:	105	-0.094	93:	109	0.229	149:	96	0.094	200:	46	0.130	251:	94	0.085	302:	95	0.168
48:	105	0.075	94:	109	0.143	150:	96	0.135	201:	47	0.213	252:	90	0.115	303:	95	0.137
49:	105	0.124	95:	109	0.049	151:	94	0.106	202:	43	0.209	253:	90	0.083	304:	94	0.093
50:	105	0.019	96:	103	0	152:	93	0.129	203:	41	0	254:	97	0.072	305:	93	0.191
51:	106	0.079	97:	101	0.109	153:	92	0.141	204:	41	0.049	255:	97	0.062	306:	93	0.129
52:	108	0.102	98:	103	-0.019	154:	90	0.187	205:	40	0	256:	97	0.062	307:	92	0.163
53:	109	0.174	99:	103	0.058	155:	95	0.146	206:	40	0.100	257:	97	-0.010	308:	93	0.129
54:	109	0.092	100:	104	0.010	156:	95	0.083	207:	41	0.098	258:	97	0.105	309:	92	0.141
55:	109	0.147	101:	104	0.019	157:	94	0.178	208:	42	0	259:	100	0.070	310:	93	0.191
56:	109	0.101	102:	103	0.029	158:	93	0.118	209:	43	0.093	260:	100	0.040	311:	93	0.140
57:	109	0.073	103:	101	0.079	159:	91	0.088	210:	63	0.048	261:	99	0.061	312:	93	0.172

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DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	3	1.000	33:	94	0.191	109:	92	0	160:	91	0.176	211:	59	0.091	262:	83	0.229
8:	19	0.333	34:	94	0.260	110:	92	-0.022	161:	91	0.220	212:	54	0.259	263:	83	0.217
9:	20	0.530	35:	94	0.234	111:	92	-0.043	162:	91	0.253	213:	59	0.271	264:	82	0.134
10:	42	0.500	36:	93	0.312	112:	92	-0.076	163:	90	0.156	214:	60	0.183	265:	83	0.293
11:	55	-0.079	37:	94	0.191	113:	91	0	164:	89	0.090	215:	60	0.117	266:	86	0.296
12:	65	-0.138	38:	95	0.211	114:	94	0.117	165:	88	0.136	216:	57	0.123	267:	89	0.195
13:	68	-0.205	39:	95	0.211	115:	94	0.165	166:	88	0.125	217:	62	0.274	268:	89	0.271
14:	76	-0.020	40:	97	0.179	116:	93	0.295	167:	89	0.101	218:	60	0.268	269:	84	0.298
15:	74	0.699	41:	98	0.092	117:	93	0.215	168:	90	0.100	219:	67	0.284	270:	89	0.294
16:	74	0.034	42:	98	-0.042	118:	93	0.065	169:	90	0.033	220:	65	0.394	271:	81	0.123
17:	78	0.013	43:	98	0.061	119:	93	0.094	170:	90	0.144	221:	60	0.374	272:	77	0.221
18:	78	-0.215	44:	98	0.071	120:	93	0.187	171:	91	0.264	222:	69	0.406	273:	87	0.293
19:	89	-0.188	45:	97	0.260	121:	95	0.208	172:	88	0.295	223:	65	0.250	274:	91	0.297
20:	89	-0.094	46:	97	0.260	122:	95	0.168	173:	88	0.307	224:	85	0.193	275:	88	0.227
21:	87	-0.161	47:	96	0.312	123:	95	0.221	174:	87	0.276	225:	87	0.310	276:	86	0.198
22:	85	0.034	48:	97	0.247	124:	94	0.191	175:	77	0.104	226:	86	0.221	277:	83	0.114
23:	86	0.057	49:	97	0.155	125:	93	0.215	176:	66	0.091	227:	89	0.105	278:	80	0.174
24:	91	0.110	50:	97	0.247	126:	93	0.151	177:	63	0.175	228:	89	0.212	279:	87	0.291
25:	92	0.054	51:	97	0.190	127:	94	0.340	178:	52	0.231	229:	83	0.217	280:	85	0.105
26:	92	0.109	52:	97	0.180	128:	93	0.387	179:	45	0.489	230:	82	0.220	281:	87	0.011
27:	92	-0.033	53:	97	0.237	129:	92	0.500	180:	32	0.125	231:	90	0.350	282:	87	0.092
28:	92	-0.022	54:	99	0.137	130:	93	0.473	181:	31	0.032	232:	91	0.335	283:	85	0.141
29:	94	0.066	55:	95	0.400	131:	93	0.366	182:	33	-0.019	233:	90	0.222	284:	85	0.141
30:	95	0.032	56:	99	0.411	132:	93	0.452	183:	52	0	234:	85	0.216	285:	83	0.145
31:	97	0.124	57:	99	0.284	133:	92	0.413	184:	51	0.157	235:	88	0.162	286:	81	0.025
32:	99	0.292	58:	94	0.138	134:	93	0.505	185:	51	0.157	236:	89	0.144	287:	82	0.073
33:	97	0.309	59:	94	0.260	135:	93	0.387	186:	50	0.020	237:	89	0.129	288:	81	0.136
34:	97	0.371	60:	93	0.204	136:	91	0.451	187:	47	0.149	238:	85	0.219	289:	81	0.198
35:	96	0.396	61:	93	0.301	137:	91	0.365	188:	44	0.136	239:	82	0.171	290:	79	0.114
36:	97	0.278	62:	92	0.239	138:	89	0.368	189:	49	0.204	240:	82	0.195	291:	81	0.173
37:	95	0.281	63:	90	0.269	139:	89	0.270	190:	49	0.122	241:	82	0.037	292:	82	0.171
38:	95	0.354	64:	90	0.111	140:	94	0.319	191:	49	0.245	242:	81	0.399	293:	82	0.220
39:	95	0.219	65:	87	0.040	141:	94	0.309	192:	50	0.120	243:	80	0.375	294:	87	0.276
40:	95	0.208	66:	91	0.341	142:	95	0.421	193:	50	0.220	244:	78	0.430	295:	80	0.244
41:	95	0.208	67:	95	0.320	143:	95	0.464	194:	48	0.187	245:	60	0.355	296:	86	0.267
42:	94	0.260	68:	96	0.469	144:	95	0.295	195:	43	0.140	246:	81	0.420	297:	80	0.105
43:	95	0.062	69:	95	0.427	145:	95	0.385	196:	45	0.200	247:	81	0.219	298:	86	0.198
44:	98	0.367	70:	96	0.333	146:	94	0.362	197:	43	0.163	248:	81	0.243	299:	87	0.241
45:	95	0.245	71:	95	0.295	147:	93	0.370	198:	42	0.048	249:	82	0.427	300:	88	0.398
46:	94	0.141	72:	96	0.167	148:	92	0.283	199:	43	0.093	250:	81	0.350	301:	88	0.386
47:	94	0.091	73:	97	0.269	149:	92	0.391	200:	42	0.095	251:	81	0.370	302:	88	0.364
48:	94	0.030	74:	97	0.195	150:	92	0.348	201:	41	-0.098	252:	84	0.393	303:	88	0.392
49:	95	0.061	75:	97	0.124	151:	93	0.237	202:	38	-0.105	253:	84	0.342	304:	88	0.443
50:	97	0.215	76:	95	0.200	152:	92	0.196	203:	41	-0.171	254:	84	0.266	305:	88	0.716
51:	97	0.062	77:	97	0.247	153:	92	0.109	204:	39	-0.205	255:	83	0.072	306:	80	0.442
52:	97	-0.082	78:	95	0.187	154:	95	0.293	205:	39	-0.231	256:	84	0.190	307:	84	0.417
53:	97	-0.010	79:	95	0.064	155:	94	0.202	206:	39	-0.256	257:	85	0.193	308:	84	0.464
54:	97	-0.021	80:	95	0.120	156:	92	0.228	207:	41	-0.171	258:	84	0.012	309:	85	0.442
55:	97	0.113	81:	94	0.043	157:	92	0.283	208:	41	-0.122	259:	85	0.141	310:	89	0.529
56:	99	0.200	82:	94	0	158:	92	0.217	209:	41	-0.098	260:	84	0.250	311:	89	0.447
57:	94	0.202	83:	92	0.070	159:	92	0.228	210:	51	0.078	261:	83	0.224	312:	89	0.412

TABLE C-4.1. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *wheezing* IN THE GROUP *CNSLD grade 0*

(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	4	0	58:	123	0.0096	109:	119	0.0078	160:	103	0.0039	211:	60	0	262:	104	-0.0029
8:	23	0	59:	123	0.0065	110:	116	0.0043	161:	104	0.0029	212:	60	0	263:	104	-0.0029
9:	38	0	60:	124	0.0069	111:	119	0.0070	162:	103	0.0029	213:	59	0	264:	103	-0.0029
10:	59	0	61:	125	0.0024	112:	116	0.0026	163:	102	0.0029	214:	59	0	265:	103	-0.0029
11:	71	0.0042	62:	123	0.0024	113:	116	0.0034	164:	102	0.0020	215:	61	0	266:	105	-0.0029
12:	82	0.0037	63:	122	0.0049	114:	117	0.0034	165:	102	0.0020	216:	62	0	267:	103	-0.0029
13:	85	0	64:	124	0.0057	115:	117	0.0026	166:	102	0.0020	217:	62	0	268:	104	-0.0029
14:	84	0	65:	121	0.0017	116:	116	0.0026	167:	97	0.0041	218:	64	0	269:	105	-0.0029
15:	94	0.0032	66:	119	0.0025	117:	115	0.0035	168:	97	0.0031	219:	65	0	270:	105	-0.0029
16:	97	0.0113	67:	120	-0.0017	118:	114	0.0035	169:	97	0.0041	220:	65	0	271:	103	-0.0029
17:	99	0.0111	68:	120	0.0017	119:	118	0.0025	170:	94	0.0032	221:	65	0	272:	102	-0.0029
18:	103	0.0087	69:	120	0.0058	120:	118	0.0025	171:	91	0.0033	222:	66	0	273:	104	-0.0029
19:	105	0.0076	70:	123	0.0065	121:	118	0.0025	172:	89	0	223:	66	0	274:	107	-0.0026
20:	106	0.0066	71:	123	0.0065	122:	118	0.0025	173:	85	0	224:	84	0.0046	275:	107	-0.0026
21:	108	0.0037	72:	123	0.0065	123:	117	0.0017	174:	85	0	225:	86	0	276:	106	-0.0028
22:	109	0.0009	73:	123	0.0065	124:	117	0.0009	175:	80	0.0050	226:	86	0	277:	107	0
23:	109	0.0009	74:	123	0.0057	125:	116	0.0009	176:	69	0	227:	86	0	278:	105	0
24:	110	0.0036	75:	123	0.0057	126:	117	0.0017	177:	63	0	228:	86	0	279:	105	0
25:	114	0.0044	76:	123	0.0057	127:	117	0.0026	178:	57	0	229:	86	0	280:	105	0.0076
26:	115	0.0009	77:	120	0.0056	128:	117	0.0017	179:	44	0	230:	86	0	281:	105	0.0076
27:	115	-0.0026	78:	120	0.0056	129:	117	0.0026	180:	38	0	231:	86	0	282:	105	0.0076
28:	116	-0.0017	79:	120	0.0056	130:	114	0.0026	181:	38	0	232:	95	0	283:	106	0
29:	116	-0.0042	80:	122	0.0057	131:	112	0.0016	182:	65	0	233:	96	0	284:	105	0
30:	116	-0.0017	81:	120	0.0056	132:	113	0.0035	183:	63	0	234:	98	-0.0041	285:	105	0
31:	122	-0.0016	82:	120	0.0050	133:	112	0.0027	184:	63	0	235:	97	-0.0041	286:	102	0
32:	122	-0.0049	83:	120	0.0050	134:	113	0.0027	185:	62	0	236:	96	0	287:	103	0.0019
33:	123	-0.0073	84:	118	0.0059	135:	113	0.0027	186:	62	0	237:	96	0	288:	103	-0.0039
34:	123	-0.0024	85:	117	0.0051	136:	113	0.0035	187:	62	0	238:	101	0	289:	103	0.0010
35:	122	-0.0008	86:	118	0.0051	137:	113	0.0035	188:	63	0	239:	100	0	290:	103	0.0010
36:	123	0.0024	87:	117	0.0060	138:	113	0.0027	189:	58	0	240:	101	0	291:	101	0
37:	124	0.0024	88:	113	0.0093	139:	112	0.0027	190:	57	0	241:	101	0	292:	100	0.0010
38:	124	0.0056	89:	112	0.0045	140:	112	0.0018	191:	57	0	242:	100	0	293:	101	0
39:	124	0.0056	90:	111	0.0036	141:	111	0.0018	192:	55	0	243:	98	0	294:	105	0
40:	124	0.0016	91:	119	0.0017	142:	111	0.0009	193:	55	0	244:	97	0	295:	104	0
41:	124	0.0024	92:	120	0.0017	143:	111	0.0009	194:	55	0	245:	100	0	296:	104	0
42:	125	-0.0032	93:	121	0.0017	144:	111	0	195:	53	0	246:	100	0	297:	105	0
43:	124	-0.0032	94:	122	0.0016	145:	111	0	196:	52	0	247:	100	0	298:	105	0
44:	124	0	95:	121	0.0017	146:	110	0	197:	53	0	248:	99	0	299:	105	0
45:	125	0.0024	96:	121	0.0017	147:	110	0	198:	55	0	249:	99	0	300:	103	0
46:	125	0.0008	97:	121	0.0017	148:	109	0	199:	56	0	250:	99	0	301:	104	0
47:	125	0.0032	98:	121	0.0008	149:	109	0	200:	56	0	251:	100	0	302:	103	0
48:	125	0.0063	99:	121	0.0008	150:	107	0.0028	201:	54	0	252:	104	0	303:	104	0
49:	125	-0.0008	100:	121	0.0008	151:	105	-0.0009	202:	51	0	253:	105	0	304:	103	0
50:	125	-0.0008	101:	121	0.0041	152:	105	0.0038	203:	52	0	254:	107	0	305:	103	0
51:	124	-0.0005	102:	121	0.0041	153:	105	0.0038	204:	53	0	255:	107	0	306:	102	0
52:	124	0	103:	121	0.0056	154:	104	0.0029	205:	52	0	256:	107	0	307:	100	0
53:	124	0.0032	104:	120	0.0050	155:	104	0.0029	206:	52	0	257:	105	0	308:	103	0
54:	124	0	105:	118	-0.0017	156:	105	0.0029	207:	52	0	258:	105	0	309:	103	0.0049
55:	123	0	106:	117	0.0026	157:	103	0.0029	208:	50	0	259:	105	-0.0029	310:	103	0
56:	125	0.0032	107:	117	0.0051	158:	103	0.0029	209:	50	0	260:	105	-0.0029	311:	102	0
57:	123	0.0057	108:	116	0.0086	159:	104	0.0029	210:	61	0	261:	104	-0.0029	312:	102	0

TABLE C-4.2. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *wheezing* IN THE GROUP *CNSLD grade 1*
(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	1	0	53:	108	0.102	109:	101	0.089	160:	89	0.011	211:	64	0.076	262:	99	0.131
8:	8	0	54:	107	0.073	110:	101	0.099	161:	90	0.067	212:	65	0	263:	96	0.125
9:	23	-0.217	55:	109	0.028	111:	101	0.069	162:	90	0.100	213:	63	0	264:	97	0.061
10:	41	-0.044	56:	109	0.020	112:	101	0.069	163:	89	0.135	214:	63	0	265:	97	0.082
11:	59	-0.085	57:	109	0.064	113:	100	0.030	164:	89	0.157	215:	64	0	266:	94	-0.074
12:	77	-0.026	58:	107	0.019	114:	103	0.058	165:	90	0.189	216:	61	0.035	267:	96	0
13:	78	-0.013	59:	106	0.047	115:	103	-0.019	166:	88	0.102	217:	71	0.070	268:	96	-0.010
14:	81	0.074	60:	106	0.069	116:	103	-0.010	167:	88	0.102	218:	74	0.027	269:	95	-0.095
15:	81	-0.037	61:	105	0.114	117:	104	-0.010	168:	89	0.045	219:	75	0	270:	98	-0.082
16:	87	0	62:	105	0.164	118:	103	0	169:	89	0.034	220:	75	0.055	271:	97	0
17:	88	0.136	63:	106	0.060	119:	106	-0.038	170:	90	0.089	221:	73	0.027	272:	94	0
18:	89	0.034	64:	106	0.065	120:	106	0	171:	88	0.136	222:	75	0.027	273:	91	-0.143
19:	93	0.065	65:	106	0.142	121:	106	0.038	172:	86	0.153	223:	75	0.034	274:	95	-0.042
20:	94	0.096	66:	106	0.115	122:	105	0.038	173:	85	0.106	224:	93	0.032	275:	96	-0.052
21:	94	0.170	67:	107	0.150	123:	104	0.038	174:	82	0.183	225:	93	0.011	276:	97	0
22:	95	0.126	68:	107	0.121	124:	105	0	175:	73	0.110	226:	93	0.075	277:	97	-0.041
23:	95	0.135	69:	106	0.028	125:	105	0.038	176:	52	0.081	227:	92	0.033	278:	97	-0.041
24:	97	0.082	70:	106	0.025	126:	104	0.035	177:	55	0.145	228:	93	0.060	279:	96	-0.083
25:	99	0.061	71:	106	0.094	127:	105	0	178:	45	0.200	229:	92	0.054	280:	94	0.032
26:	101	0.069	72:	106	0.075	128:	104	0	179:	41	0.195	230:	92	0.054	281:	94	-0.021
27:	101	0.030	73:	107	0.103	129:	105	0.038	180:	33	0.091	231:	94	0.053	282:	95	-0.042
28:	102	0.137	74:	107	0.037	130:	105	0.029	181:	31	0	232:	94	-0.043	283:	95	-0.042
29:	101	0.089	75:	107	0.037	131:	105	0.017	182:	54	0	233:	94	-0.117	284:	95	-0.042
30:	101	0.050	76:	108	0.023	132:	106	0.047	183:	54	0	234:	92	-0.065	285:	94	-0.074
31:	102	0.108	77:	108	0.037	133:	107	0.043	184:	53	0.075	235:	93	0.011	286:	89	-0.045
32:	101	0.144	78:	108	0	134:	107	0.075	185:	53	0	236:	92	0.065	287:	88	0.045
33:	101	0.119	79:	107	0.028	135:	107	0.065	186:	52	0.077	237:	91	0.071	288:	88	0.023
34:	101	0.079	80:	107	0.028	136:	106	0.066	187:	52	0	238:	94	0.065	289:	88	0.023
35:	106	0.047	81:	106	0.019	137:	105	0.029	188:	52	0.077	239:	94	0.043	290:	89	0
36:	105	0.086	82:	105	0.029	138:	103	0	189:	55	0.036	240:	94	0.021	291:	88	0
37:	105	0.066	83:	104	0.096	139:	104	0	190:	56	0.071	241:	94	0.065	292:	88	-0.011
38:	106	0.094	84:	104	0.163	140:	103	0.039	191:	55	0	242:	93	0.022	293:	88	-0.057
39:	107	0.093	85:	104	0.135	141:	105	0.086	192:	55	0	243:	90	0.050	294:	93	0
40:	107	0.103	86:	104	0.038	142:	104	0.087	193:	55	0	244:	89	0.045	295:	94	0
41:	107	0.140	87:	105	0.047	143:	103	0.078	194:	54	0	245:	93	0	296:	94	0
42:	108	0.139	88:	107	0.019	144:	102	0.049	195:	51	0.039	246:	93	0.032	297:	93	0.011
43:	108	0.130	89:	108	-0.020	145:	101	0.050	196:	48	0.062	247:	94	0.045	298:	93	0.054
44:	108	0.056	90:	108	0.028	146:	99	0.091	197:	47	0.064	248:	95	0.137	299:	93	0.054
45:	107	-0.009	91:	106	-0.019	147:	97	0.093	198:	47	0.128	249:	96	0.115	300:	93	0.011
46:	107	0.009	92:	105	0.067	148:	97	0.062	199:	47	0.106	250:	95	0.108	301:	95	0.053
47:	106	0.038	93:	105	-0.019	149:	96	0.083	200:	46	0.065	251:	94	0.170	302:	95	0.064
48:	105	0.105	94:	105	0.067	150:	96	0.052	201:	47	0.064	252:	96	0.167	303:	95	0.064
49:	105	0.010	95:	103	0.019	151:	94	0.085	202:	43	0.070	253:	96	0.073	304:	94	0.011
50:	105	0.029	96:	103	-0.029	152:	93	0.075	203:	41	0.073	254:	97	0.041	305:	93	0.065
51:	106	0.075	97:	101	-0.069	153:	92	0.076	204:	41	0.122	255:	97	0.062	306:	93	-0.032
52:	106	0.026	98:	103	-0.039	154:	96	0.083	205:	40	0.075	256:	97	0.103	307:	92	0.109
53:	109	0.037	99:	103	-0.024	155:	95	0.062	206:	40	0.075	257:	97	0.041	308:	93	0.075
54:	108	0.065	100:	104	0.019	156:	96	0.042	207:	41	0.073	258:	97	0.045	309:	93	0.022
55:	109	0.055	101:	104	0.029	157:	94	0.064	208:	42	0.071	259:	100	0.020	310:	93	-0.011
56:	109	0.073	102:	103	0.039	158:	93	0.032	209:	43	0.116	260:	100	0.070	311:	93	-0.011
57:	109	0.110	103:	101	0.119	159:	91	0.022	210:	63	0.032	261:	99	0.081	312:	93	-0.043

TABLE C-4.3. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *wheezing* IN THE GROUP *CNSLD grade 2+3*

(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	3	-1.333	54:	94	0.287	109:	91	0.033	160:	90	0.100	211:	95	0.091	262:	83	0.265	313:	84	0.107	
8:	15	-0.267	55:	94	0.245	110:	91	-0.022	161:	90	0.256	212:	94	0.130	263:	83	0.337	314:	85	0.153	
9:	26	-0.077	60:	94	0.267	111:	91	-0.022	162:	90	0.233	213:	94	0.237	264:	82	0.266	315:	84	0.155	
10:	42	0.214	61:	93	0.183	112:	91	0.044	163:	89	0.101	214:	60	0.283	265:	83	0.265	316:	84	0.140	
11:	53	-0.189	62:	94	0.160	113:	90	0.044	164:	88	0.034	215:	60	0.100	266:	86	0.186	317:	84	0.179	
12:	65	-0.200	63:	95	0.147	114:	93	0.032	165:	87	0	216:	57	0.158	267:	85	0.200	318:	83	0.181	
13:	68	-0.235	64:	95	0.095	115:	93	0.011	166:	87	0.023	217:	62	0.161	268:	85	0.200	319:	85	0.035	
14:	70	-0.066	65:	96	0.052	116:	94	0.053	167:	88	0.034	218:	66	0.227	269:	84	0.202	320:	86	-0.015	
15:	74	0.014	66:	95	0.092	117:	92	0.033	168:	89	0	219:	67	0.254	270:	85	0.141	321:	87	0.034	
16:	74	0.054	67:	98	0.031	118:	92	0.022	169:	89	0.034	220:	66	0.242	271:	81	0	322:	85	0.012	
17:	77	0.234	68:	98	0.224	119:	95	0.063	170:	90	0.078	221:	67	0.269	272:	77	0.026	323:	86	0.047	
18:	77	0.026	69:	98	0.082	120:	95	0.137	171:	90	0.133	222:	69	0.261	273:	87	0.080	324:	86	0.093	
19:	84	0	70:	97	0.072	121:	94	0.138	172:	87	0.149	223:	68	0.147	274:	91	0.253	325:	85	0.188	
20:	85	-0.024	71:	97	0.062	122:	94	0.106	173:	87	0.149	224:	65	0.082	275:	88	0.261	326:	85	0.176	
21:	87	0.264	72:	96	0.150	123:	94	0.106	174:	86	0.105	225:	87	0.161	276:	87	0.184	327:	85	0.141	
22:	87	0.068	73:	97	0.093	124:	93	0.129	175:	76	0	226:	86	0.209	277:	88	0.159	328:	85	0.165	
23:	88	0.045	74:	97	0.061	125:	92	0.185	176:	65	0.062	227:	86	0.186	278:	87	0.149	329:	86	0.221	
24:	91	0.077	75:	97	0.032	126:	92	0.174	177:	62	0.048	228:	85	0.247	279:	87	0.216	330:	87	0.042	
25:	92	0.098	76:	97	0.072	127:	93	0.172	178:	52	0.135	229:	83	0.241	280:	86	0.233	331:	86	0.058	
26:	92	0.054	77:	97	0.113	128:	93	0.172	179:	45	0.333	230:	82	0.199	281:	87	0.184	332:	85	0.059	
27:	92	0	78:	97	0.134	129:	91	0.077	180:	32	0.125	231:	90	0.244	282:	87	0.218	333:	84	0.119	
28:	92	-0.022	79:	95	0.168	130:	92	0.228	181:	31	0.161	232:	91	0.264	283:	85	0.118	334:	85	0.118	
29:	93	-0.022	80:	95	0.305	131:	92	0.152	182:	53	0.075	233:	89	0.157	284:	85	0.141	335:	85	0.047	
30:	95	-0.011	81:	95	0.242	132:	92	0.207	183:	52	0.154	234:	88	0.170	285:	83	0.072	336:	84	0.107	
31:	97	0.103	82:	95	0.147	133:	91	0.319	184:	51	0.235	235:	88	0.136	286:	80	0.037	337:	83	0.120	
32:	96	0.135	83:	94	-0.053	134:	92	0.337	185:	51	0.235	236:	89	0.191	287:	82	0.098	338:	83	0.181	
33:	97	0.247	84:	94	0.089	135:	92	0.293	186:	50	0.220	237:	89	0.262	288:	80	0.200	339:	83	0.217	
34:	97	0.144	85:	93	0.066	136:	90	0.333	187:	47	0.191	238:	85	0.271	289:	81	0.222	340:	83	0.169	
35:	96	0.135	86:	93	0	137:	90	0.289	188:	44	0.136	239:	82	0.293	290:	79	0.177	341:	83	0.193	
36:	97	0.103	87:	92	0.098	138:	88	0.261	189:	49	0.224	240:	82	0.244	291:	80	0.162	342:	83	0.325	
37:	96	0.115	88:	90	-0.078	139:	89	0.247	190:	49	0.184	241:	82	0.305	292:	82	0.073	343:	84	0.214	
38:	96	0.229	89:	90	0	140:	93	0.237	191:	49	0.224	242:	81	0.444	293:	82	0.134	344:	83	0.229	
39:	95	0.105	90:	87	0.034	141:	93	0.172	192:	50	0.180	243:	80	0.413	294:	87	0.115	345:	83	0.181	
40:	95	0.167	91:	90	0.167	142:	94	0.202	193:	50	0.260	244:	78	0.399	295:	86	0.081	346:	82	0.195	
41:	95	0.115	92:	94	0.161	143:	94	0.234	194:	48	0.271	245:	80	0.288	296:	86	0.093	347:	83	0.157	
42:	96	0.146	93:	95	0.179	144:	93	0.258	195:	43	0.256	246:	81	0.259	297:	86	0.070	348:	83	0.157	
43:	96	0.140	94:	95	0.211	145:	95	0.337	196:	45	0.133	247:	81	0.346	298:	86	0.186	349:	82	0.171	
44:	96	0.186	95:	95	0.168	146:	93	0.323	197:	43	0.047	248:	81	0.370	299:	87	0.218	350:	80	0.137	
45:	96	0.153	96:	94	0.128	147:	92	0.370	198:	42	0.095	249:	81	0.469	300:	87	0.299	351:	87	0.134	
46:	99	0.111	77:	95	0.042	148:	92	0.348	199:	43	0.070	250:	81	0.264	301:	86	0.261	352:	87	0.158	
47:	99	0.040	98:	96	0.021	149:	91	0.352	200:	42	0.024	251:	81	0.222	302:	86	0.261	353:	42	0.311	
48:	99	0.081	99:	96	-0.031	150:	91	0.264	201:	41	0.049	252:	84	0.226	303:	88	0.261	354:	32	0.312	
49:	98	0	100:	95	0.053	151:	92	0.185	202:	38	0.079	253:	84	0.250	304:	88	0.341	355:	21	0.667	
50:	97	0.072	101:	94	0.011	152:	91	0.220	203:	41	-0.073	254:	84	0.250	305:	88	0.420	356:	15	0.467	
51:	97	0.041	102:	96	-0.021	153:	91	0.209	204:	39	0	255:	83	0.349	306:	86	0.267	357:	11	0.273	
52:	97	-0.082	103:	95	-0.032	154:	94	0.255	205:	39	-0.026	256:	84	0.226	307:	84	0.226	358:	10	0.300	
53:	97	0.010	104:	94	-0.021	155:	92	0.293	206:	39	-0.051	257:	85	0.212	308:	85	0.259	359:	10	0.300	
54:	97	0.031	105:	93	0.054	156:	91	0.330	207:	41	-0.098	258:	84	0.190	309:	86	0.291	360:	10	0.300	
55:	97	0.062	106:	93	-0.032	157:	91	0.187	208:	41	0	259:	85	0.306	310:	86	0.291	361:	8	0.375	
56:	95	0.021	107:	93	-0.086	158:	91	0.231	209:	41	-0.024	260:	84	0.226	311:	85	0.185	362:	7	0.429	
57:	94	0.053	108:	91	-0.033	159:	91	0.143	210:	51	0.078	261:	83	0.325	312:	85	0.153	363:	2	1.950	

TABLE C-5.1. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *irritation of the eyes* IN THE GROUP CNSLD grade 0
(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY			DAY			DAY			DAY			DAY			DAY			DAY		
N	DIFF.		N	DIFF.		N	DIFF.		N	DIFF.		N	DIFF.		N	DIFF.		N	DIFF.	
7:	4	0	58:	123	0	109:	115	-0.0343	160:	103	0.019	211:	60	-0.067	262:	104	-0.077	313:	102	0.078
8:	23	0	59:	123	-0.006	110:	115	-0.034	161:	104	0.048	212:	60	-0.067	263:	104	-0.067	314:	100	0.060
9:	38	0.184	60:	124	-0.024	111:	115	-0.070	162:	103	0.039	213:	59	0.017	264:	103	-0.049	315:	103	0.078
10:	59	-0.068	61:	124	-0.065	112:	115	-0.069	163:	102	0.078	214:	59	0	265:	103	-0.076	316:	103	0.078
11:	71	0.042	62:	123	-0.057	113:	116	-0.069	164:	102	0.078	215:	61	-0.049	266:	103	-0.048	317:	103	0.078
12:	82	0.012	63:	122	-0.033	114:	117	-0.034	165:	102	0.078	216:	62	0.017	267:	103	-0.078	318:	102	0.078
13:	86	-0.047	64:	122	-0.041	115:	117	0	166:	102	0.078	217:	62	-0.046	268:	104	-0.014	319:	102	0.049
14:	89	0.067	65:	121	-0.066	116:	115	0.009	167:	97	0.124	218:	64	-0.062	269:	103	0.010	320:	102	0.069
15:	94	0.032	66:	119	-0.042	117:	115	0.017	168:	97	0.052	219:	65	-0.062	270:	103	-0.049	321:	102	0.069
16:	97	-0.021	67:	120	-0.066	118:	114	-0.018	169:	97	0.093	220:	65	-0.062	271:	103	-0.024	322:	102	0.078
17:	99	-0.040	68:	120	-0.033	119:	113	-0.034	170:	94	0.085	221:	65	-0.062	272:	101	-0.030	323:	102	0.069
18:	103	-0.087	69:	120	-0.067	120:	117	0.034	171:	91	0.088	222:	65	-0.061	273:	104	0.010	324:	102	0
19:	105	-0.019	70:	123	0.057	121:	118	0.068	172:	89	0.045	223:	65	-0.061	274:	107	0.009	325:	101	0.040
20:	106	-0.075	71:	123	0.041	122:	118	0.034	173:	85	0.047	224:	64	0.036	275:	106	0.009	326:	102	0.049
21:	109	-0.110	72:	123	0	123:	117	0.026	174:	85	0	225:	65	0.035	276:	106	0.009	327:	102	-0.029
22:	108	-0.102	73:	123	0.024	124:	117	0.060	175:	80	0.050	226:	65	0.035	277:	107	0.004	328:	101	-0.059
23:	109	0	74:	123	0.033	125:	116	0.060	176:	69	0.174	227:	65	0.047	278:	104	0.038	329:	100	0
24:	110	0.027	75:	123	0	126:	117	0	177:	63	0.222	228:	65	-0.012	279:	105	0.007	330:	99	0.040
25:	113	-0.009	76:	123	0	127:	117	0.026	178:	57	0.070	229:	65	0.061	280:	105	0.038	331:	99	0.040
26:	115	0	77:	120	0.005	128:	117	0.051	179:	44	-0.114	230:	65	0.035	281:	105	0.019	332:	99	0.040
27:	115	-0.122	78:	120	-0.025	129:	117	0.094	180:	38	0	231:	65	0.036	282:	105	0.067	333:	99	0
28:	119	-0.050	79:	120	0	130:	114	0.132	181:	38	-0.105	232:	97	-0.011	283:	106	0.004	334:	101	0

TABLE C-5.2. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *irritation of the eyes* IN THE GROUP *CNSLD grade 1*
(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	1	0	54:	106	0.085	109:	100	0.080	160:	89	0.258	211:	64	0.031	262:	99	0.030
8:	8	0	55:	109	0.018	110:	101	0.119	161:	90	0.211	212:	60	0.031	263:	96	0.010
9:	23	-0.217	56:	109	0.046	111:	100	0.080	162:	90	0.200	213:	63	0.032	264:	97	0.144
10:	41	-0.266	57:	109	0.147	112:	100	0.150	163:	89	0.191	214:	63	0.092	265:	97	0.010
11:	59	-0.051	58:	109	0.147	113:	100	0.190	164:	89	0.112	215:	64	0.094	266:	94	0.011
12:	77	-0.052	59:	107	0.084	114:	103	0.078	165:	90	0.244	216:	61	0.066	267:	96	-0.010
13:	79	0.101	60:	106	0.038	115:	103	0.029	166:	88	0.261	217:	71	0.056	268:	96	-0.031
14:	81	0.037	61:	106	0.170	116:	103	0.136	167:	88	0.216	218:	74	-0.014	269:	95	0.011
15:	81	0.025	62:	106	0.104	117:	104	0.125	168:	87	0.322	219:	75	-0.013	270:	98	-0.153
16:	87	0.172	63:	106	0.009	118:	103	0.135	169:	90	0.289	220:	75	0.067	271:	97	-0.062
17:	88	0.227	64:	106	0.094	119:	105	0.152	170:	90	0.300	221:	73	-0.014	272:	94	0.021
18:	89	0.067	65:	106	0.094	120:	106	0.142	171:	88	0.318	222:	75	0.027	273:	91	-0.033
19:	93	0	66:	106	0.151	121:	106	0.104	172:	86	0.326	223:	76	0.053	274:	95	0.021
20:	94	0.125	67:	106	0.179	122:	105	0.105	173:	85	0.329	224:	92	0.120	275:	96	0.062
21:	94	-0.043	68:	107	0.202	123:	105	0.133	174:	82	0.390	225:	93	0.097	276:	97	0.052
22:	95	0.063	69:	107	0.064	124:	105	0.038	175:	73	0.329	226:	93	0.097	277:	97	0.103
23:	96	0.062	70:	106	0.094	125:	105	0.057	176:	62	0.323	227:	92	0.130	278:	97	0.010
24:	97	0.124	71:	106	0.132	126:	104	0.125	177:	55	0.600	228:	92	0.141	279:	96	0.062
25:	99	0.162	72:	105	0.019	127:	105	0.114	178:	45	0.356	229:	92	0.067	280:	94	0.149
26:	101	0.178	73:	106	0.123	128:	104	0.115	179:	41	0.268	230:	92	0.087	281:	95	0.064
27:	101	-0.089	74:	107	0.025	129:	105	0.114	180:	33	0.333	231:	94	0.053	282:	95	0.021
28:	102	0.029	75:	107	0.009	130:	105	0.086	181:	31	0.161	232:	94	-0.032	283:	95	-0.095
29:	101	0.064	76:	107	0.306	131:	106	0.094	182:	54	0.074	233:	94	0.053	284:	95	0.042
30:	101	0.059	77:	108	0.250	132:	106	0.075	183:	54	0.093	234:	92	0.011	285:	94	0.032
31:	102	0.029	78:	108	0.074	133:	107	0.075	184:	53	0.019	235:	93	0.011	286:	69	0.090
32:	102	0.195	79:	109	-0.092	134:	107	0.112	185:	53	0.189	236:	92	-0.011	287:	68	0.148
33:	102	0.137	80:	107	0.075	135:	107	0.178	186:	52	0.038	237:	91	0.095	288:	88	0.068
34:	102	0.118	81:	107	0.163	136:	106	0.208	187:	52	0.038	238:	94	0.064	289:	88	0.057
35:	106	0.094	82:	106	0.132	137:	105	0.105	188:	52	0.096	239:	94	0.105	290:	89	0.090
36:	105	0.133	83:	105	0.246	138:	103	0.078	189:	54	0.167	240:	94	0.065	291:	88	0.159
37:	105	-0.010	84:	104	0.163	139:	104	0.125	190:	55	0.143	241:	94	0.223	292:	88	0.125
38:	106	0.089	85:	104	0.250	140:	103	0.155	191:	55	0	242:	93	0.075	293:	87	0.149
39:	107	-0.028	86:	104	0.154	141:	105	0.200	192:	55	0	243:	90	0.100	294:	93	0.129
40:	107	0.009	87:	104	0.154	142:	104	0.125	193:	55	-0.073	244:	90	0.044	295:	93	0.226
41:	107	0.103	88:	105	0.060	143:	103	0.146	194:	54	-0.074	245:	93	0.065	296:	94	-0.011
42:	108	0.028	89:	107	0.103	144:	102	0.147	195:	51	-0.078	246:	92	0.098	297:	93	0.075
43:	108	-0.009	90:	108	0.204	145:	101	0.099	196:	48	0	247:	94	0.266	298:	93	0.108
44:	108	-0.009	91:	108	0.189	146:	99	0.121	197:	47	-0.085	248:	95	0.356	299:	92	0.011
45:	107	0.112	92:	106	0.151	147:	97	0.206	198:	47	0	249:	95	0.206	300:	93	0.043
46:	107	0.075	93:	105	0.171	148:	97	0.206	199:	47	0.085	250:	95	0.137	301:	95	0.084
47:	106	0	94:	104	0.139	149:	96	0.219	200:	46	0	251:	94	0.074	302:	95	0.021
48:	105	0.048	95:	105	0.229	150:	96	0.177	201:	47	0	252:	96	0.021	303:	95	-0.011
49:	105	0.010	96:	103	0.169	151:	94	0.202	202:	43	0	253:	96	0.010	304:	94	0.064
50:	105	0.076	97:	103	0.078	152:	93	0.258	203:	41	0	254:	97	0.021	305:	93	0.183
51:	106	0.113	98:	102	0.089	153:	92	0.141	204:	41	-0.024	255:	97	0.021	306:	93	0.247
52:	106	0	99:	103	0.146	154:	96	0.219	205:	40	0	256:	96	0.083	307:	92	0.228
53:	109	0.101	100:	103	0.146	155:	96	0.167	206:	40	0	257:	97	-0.021	308:	93	0.151
54:	108	0.074	101:	103	0.146	156:	95	0.211	207:	41	0	258:	97	0.041	309:	91	0.110
55:	109	0.119	102:	104	0.096	157:	94	0.213	208:	42	0.095	259:	100	0.090	310:	93	0.118
56:	109	0.156	103:	103	0.146	158:	93	0.204	209:	43	0.093	260:	100	-0.040	311:	93	0.118
57:	109	0.101	104:	101	0.090	159:	91	0.253	210:	63	0.095	261:	99	-0.091	312:	93	0.097

TABLE C-5.3. THE DAILY MEAN SCORE-DIFFERENCE WITH RESPECT TO THE SYMPTOM *irritation of the eyes* IN THE GROUP CNSLD grade 2+3.
(N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:	3	0	58:	94	0.032	109:	90	-0.022	160:	90	0.011	211:	55	-0.145	262:	83	0.035
8:	15	0	59:	94	-0.043	110:	91	-0.132	161:	90	-0.111	212:	54	0.093	263:	83	0.106
9:	26	-0.038	60:	94	0.074	111:	91	0.088	162:	90	-0.122	213:	59	0.193	264:	83	0.024
10:	42	0.071	61:	93	0.043	112:	91	0.022	163:	89	-0.056	214:	60	0.090	265:	83	-0.084
11:	53	-0.094	62:	94	-0.064	113:	90	0.033	164:	88	0.034	215:	60	0.067	266:	86	0.093
12:	65	0.042	63:	95	0.042	114:	93	-0.032	165:	87	0	216:	50	0.054	267:	89	0.012
13:	68	-0.029	64:	95	-0.021	115:	93	-0.065	166:	87	-0.069	217:	61	0	268:	89	0.062
14:	75	-0.025	65:	97	-0.041	116:	94	0.170	167:	88	0.023	218:	65	0.015	269:	84	0.135
15:	74	0.135	66:	98	-0.092	117:	93	0.043	168:	89	-0.011	219:	66	0.015	270:	89	0.217
16:	73	0.137	67:	98	-0.031	118:	93	0.086	169:	89	0.056	220:	65	0.062	271:	81	0.185
17:	78	0.115	68:	98	-0.020	119:	95	0.011	170:	90	0.100	221:	66	-0.050	272:	77	0.013
18:	78	0.141	69:	98	-0.112	120:	95	0.032	171:	90	0.044	222:	68	-0.068	273:	87	-0.069
19:	85	0.118	70:	97	0.072	121:	95	-0.042	172:	87	0.092	223:	69	0.059	274:	91	-0.033
20:	85	0.153	71:	97	0.052	122:	94	-0.043	173:	87	0.057	224:	85	-0.024	275:	87	0.034
21:	87	-0.057	72:	98	-0.010	123:	94	-0.074	174:	86	0.047	225:	87	0.023	276:	87	0.060
22:	88	0.159	73:	97	-0.093	124:	94	-0.032	175:	76	-0.053	226:	86	0.105	277:	88	0.159
23:	85	-0.034	74:	97	-0.031	125:	92	-0.022	176:	65	-0.015	227:	85	-0.035	278:	87	0.164
24:	91	0.198	75:	97	-0.103	126:	92	0.055	177:	51	0.197	228:	85	0.035	279:	87	0.207
25:	92	-0.011	76:	97	0.062	127:	93	0.140	178:	52	0.212	229:	83	0.325	280:	86	0.151
26:	92	0.153	77:	97	0	128:	93	-0.054	179:	45	0.311	230:	53	-0.012	281:	87	0.207
27:	92	0.109	78:	97	0.062	129:	91	0	180:	32	0	231:	90	0.044	282:	87	0.241
28:	93	0.011	79:	95	0.116	130:	92	0	181:	31	-0.032	232:	91	0.033	283:	85	0.294
29:	94	0	80:	95	0.400	131:	92	-0.033	182:	53	0.075	233:	90	0.011	284:	85	0.106
30:	97	-0.126	81:	95	0.274	132:	92	-0.033	183:	52	0.096	234:	88	0.102	285:	83	0.253
31:	97	0.052	82:	95	0.684	133:	91	0.110	184:	51	-0.118	235:	88	0.045	286:	81	0.012
32:	96	-0.094	83:	94	-0.074	134:	92	0.109	185:	51	0.078	236:	88	0.091	287:	82	0.122
33:	97	0.299	84:	93	-0.043	135:	92	0.076	186:	50	-0.060	237:	86	0.047	288:	81	0.066
34:	97	0.227	85:	93	0.118	136:	90	-0.111	187:	47	-0.085	238:	85	-0.012	289:	81	0
35:	97	0.196	86:	93	0.065	137:	90	0.066	188:	44	-0.023	239:	82	-0.012	290:	79	-0.036
36:	97	0.216	87:	92	0.109	138:	85	0.193	189:	49	0.102	240:	81	0	291:	81	-0.049
37:	95	0.031	88:	90	0.089	139:	86	0.170	190:	49	0.163	241:	82	0.110	292:	82	0.046
38:	95	0.083	89:	90	0.067	140:	93	0.172	191:	49	0.061	242:	81	0.049	293:	82	0.122
39:	96	0.073	90:	87	0.011	141:	93	0.043	192:	50	-0.100	243:	80	0.075	294:	87	0.103
40:	96	0.052	91:	90	0.169	142:	94	0	193:	50	0.080	244:	75	0	295:	86	-0.035
41:	95	0.126	92:	94	0.021	143:	94	0.106	194:	48	-0.042	245:	79	-0.063	296:	85	0.047
42:	95	-0.032	93:	95	0.074	144:	93	0.075	195:	43	0.070	246:	81	-0.049	297:	87	0.230
43:	95	0.010	94:	95	0.165	145:	95	0.095	196:	45	-0.111	247:	81	0.321	298:	86	0.035
44:	96	0.173	95:	95	0.105	146:	93	0.032	197:	43	-0.186	248:	81	0.370	299:	87	0.136
45:	95	-0.051	96:	94	0.136	147:	92	0.076	198:	42	-0.095	249:	82	0.159	300:	87	0.034
46:	99	0.020	97:	95	-0.021	148:	92	0.152	199:	43	0	250:	81	0.123	301:	86	0.034
47:	94	-0.131	98:	96	-0.042	149:	91	0.055	200:	41	0.024	251:	81	0.049	302:	86	0.060
48:	98	0.061	99:	95	-0.011	150:	91	0.055	201:	41	-0.146	252:	84	0.046	303:	86	0.125
49:	98	0.071	100:	96	0.062	151:	92	0.130	202:	38	-0.144	253:	85	0.047	304:	88	0.170
50:	97	0.237	101:	94	0.064	152:	91	0.187	203:	41	-0.317	254:	84	-0.012	305:	88	0.375
51:	97	0.082	102:	96	0.010	153:	91	0.055	204:	39	-0.333	255:	82	-0.134	306:	85	0.447
52:	97	0.031	103:	95	0.042	154:	94	0.074	205:	39	-0.256	256:	83	0.133	307:	84	0.333
53:	97	-0.052	104:	94	0.090	155:	93	0.129	206:	38	-0.184	257:	84	0.036	308:	82	0.235
54:	97	-0.113	105:	93	0.043	156:	91	0.143	207:	41	-0.171	258:	84	0.024	309:	85	0.062
55:	97	0.072	106:	93	-0.080	157:	90	0.067	208:	41	-0.146	259:	85	0.047	310:	86	0.105
56:	95	0.042	107:	93	-0.118	158:	91	0.011	209:	41	-0.244	260:	84	0.063	311:	85	-0.024
57:	94	-0.117	108:	91	-0.044	159:	91	0.011	210:	51	-0.020	261:	82	-0.012	312:	85	0.024

TABLE C-6.1. THE DAILY MEAN OF THE DIFFERENCES IN "PERCENTAGE DIFFERENCE FROM THE MEAN" WITH RESPECT TO
THE peak flow values IN THE GROUP CNSLD grade 0 (N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:			58:			109:	6	-0.124	160:			211:	2	0.069	262:	18	0.012
8:			59:			110:	2	0.162	161:			212:			263:	15	0.032
9:			60:			111:			162:			213:	5	-0.019	264:	7	-0.014
10:			61:			112:			163:	8	-0.005	214:	3	-0.041	265:		
11:			62:			113:			164:	13	0.011	215:	2	-0.047	266:		
12:			63:			114:	8	0.035	165:	7	0.026	216:			267:	14	0.006
13:			64:			115:	11	-0.063	166:	4	0.013	217:			268:	19	-0.004
14:			65:			116:	6	-0.091	167:			218:	9	0.073	269:	20	-0.034
15:			66:			117:	7	0.065	168:			219:	5	-0.001	270:	16	-0.025
16:			67:			118:			169:	14	-0.033	220:	8	-0.009	271:	5	0.028
17:			68:			119:			170:	7	0.030	221:	6	-0.013	272:		
18:			69:			120:			171:	3	-0.017	222:	6	-0.016	273:		
19:			70:			121:	7	0.059	172:	5	0.049	223:			274:	19	0.013
20:			71:			122:	8	0.050	173:	4	0.038	224:			275:	12	-0.014
21:			72:			123:	5	-0.084	174:			225:	13	-0.023	276:	16	-0.002
22:			73:			124:	6	0.018	175:			226:	7	-0.026	277:	16	-0.005
23:			74:			125:			176:	11	0.015	227:	9	-0.026	278:	9	0.011
24:			75:			126:			177:	12	-0.003	228:	13	-0.011	279:		
25:			76:			127:	8	0.003	178:	7	0.037	229:	9	0.009	280:		
26:			77:			128:	9	-0.022	179:	9	0.002	230:			281:	17	-0.020
27:			78:			129:	12	0.051	180:	5	0.021	231:			282:	10	0.032
28:			79:			130:	5	-0.025	181:			232:	13	0.029	283:	17	-0.039
29:			80:			131:	9	-0.012	182:			233:	10	0.034	284:	15	0.048
30:			81:			132:			183:			234:	14	-0.025	285:	7	0.011
31:			82:			133:			184:			235:	15	-0.020	286:		
32:			83:			134:	19	0.033	185:			236:	10	-0.006	287:		
33:			84:			135:	18	-0.012	186:			237:			288:	9	0.031
34:			85:			136:	24	0.052	187:			238:			289:	13	0.050
35:			86:			137:	14	0.024	188:			239:	12	0.055	290:	11	-0.006
36:			87:			138:	5	0.004	189:			240:	11	-0.021	291:	13	-0.023
37:			88:			139:			190:			241:	16	0.002	292:	6	-0.160
38:			89:			140:			191:			242:	15	0.015	293:		
39:			90:			141:	17	0.041	192:			243:	9	0.041	294:		
40:			91:			142:	20	0.007	193:			244:			295:	17	-0.014
41:			92:	7	0.086	143:	18	-0.011	194:			245:			296:	19	0.007
42:			93:	8	-0.006	144:	16	0.026	195:			246:	14	-0.042	297:	18	-0.025
43:			94:	7	-0.029	145:	8	-0.017	196:			247:	11	-0.016	298:	14	-0.028
44:			95:	5	-0.003	146:			197:			248:			299:	7	-0.009
45:			96:	6	0.086	147:			198:			249:	15	-0.027	300:		
46:			97:			148:	16	0.045	199:			250:	10	0.006	301:		
47:			98:			149:	18	0.009	200:			251:			302:	16	0.024
48:			99:	10	-0.031	150:	20	0.011	201:			252:			303:	13	0.025
49:			100:	5	0.009	151:			202:			253:	15	-0.042	304:	13	-0.024
50:			101:	11	0.039	152:	3	-0.066	203:			254:	16	-0.018	305:	16	-0.013
51:			102:	4	0.026	153:			204:			255:	13	-0.010	306:	6	-0.010
52:			103:	7	0.086	154:			205:			256:	22	0.023	307:		
53:			104:			155:	19	0.014	206:			257:	10	-0.015	308:		
54:			105:			156:	15	-0.026	207:			258:			309:	15	0.004
55:			106:	10	0.053	157:	14	-0.032	208:			259:			310:	16	0.029
56:			107:	11	0.063	158:	13	-0.018	209:			260:	18	-0.053	311:	20	0.006
57:			108:	9	0.051	159:	6	0.020	210:			261:	16	-0.042	312:	14	-0.016

TABLE C-6.2. THE DAILY MEAN OF THE DIFFERENCES IN "PERCENTAGE DIFFERENCE FROM THE MEAN" WITH RESPECT TO
THE peak flow values IN THE GROUP CNSLD grade 1 (N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:			54:			109:	7	0.028	160:			211:	12	0.046	313:	15	-0.012
8:			55:			110:	7	0.052	161:			212:	1	-0.077	314:	10	0.001
9:			60:			111:			162:			213:	2	0.056	315:		
10:			61:			112:			163:	6	0.066	214:	4	0.161	316:	17	-0.013
11:			62:			113:			164:	5	0.038	215:	6	0.039	317:	12	-0.010
12:			63:			114:	8	0.034	165:	2	0.049	216:			318:	10	-0.118
13:			64:			115:	10	-0.017	166:	5	-0.060	217:			319:	7	0.017
14:			65:			116:	9	0.051	167:			218:	8	0.081	320:	14	-0.026
15:			66:			117:	12	0.019	168:			219:	6	-0.020	321:		
16:			67:			118:			169:	7	0.032	220:	3	0.031	322:		
17:			68:			119:			170:	5	-0.007	221:	5	0.001	323:	14	0.063
18:			69:			120:			171:	1	-0.034	222:	10	0.012	324:	11	0.028
19:			70:			121:	10	0.015	172:	2	0.111	223:			325:	10	-0.002
20:			71:			122:	12	0.040	173:	2	-0.027	224:			326:	9	-0.064
21:			72:			123:	12	0.021	174:			225:	12	0.015	327:	17	-0.007
22:			73:			124:	14	0.015	175:			226:	10	0.011	328:		
23:			74:			125:			176:	6	-0.100	227:	9	-0.038	329:		
24:			75:			126:			177:	5	0.004	228:	9	0.069	330:	19	0.029
25:			76:			127:	16	-0.010	178:	6	-0.012	229:	11	0.069	331:	15	0.018
26:			77:			128:	11	-0.015	179:	5	0.007	230:			332:	28	-0.018
27:			78:			129:	11	0.056	180:	4	0.049	231:			333:	8	0.011
28:			79:			130:	15	-0.006	181:			232:	14	0.010	334:	13	0.007
29:			80:			131:	18	-0.006	182:			233:	14	0.015	335:		
30:			81:			132:			183:			234:	8	-0.028	336:		
31:			82:			133:			184:			235:	6	-0.014	337:	13	-0.006
32:			83:			134:	12	-0.035	185:			236:	15	0.013	338:	11	0.026
33:			84:			135:	10	0.018	186:			237:			339:	1	0.077
34:			85:			136:	10	0.030	187:			238:			340:	9	-0.040
35:			86:			137:	8	0.041	188:			239:	14	-0.007	341:	9	-0.060
36:			87:			138:	13	0.039	189:			240:	15	0.032	342:		
37:			88:			139:			190:			241:	8	0.027	343:		
38:			89:			140:			191:			242:	8	0.032	344:	7	0.035
39:			90:			141:	9	-0.040	192:			243:	11	0.036	345:	10	0.038
40:			91:			142:	16	-0.056	193:			244:			346:	15	-0.022
41:			92:	9	-0.007	143:	14	-0.032	194:			245:			347:	8	-0.007
42:			93:	12	-0.049	144:	14	0.003	195:			246:	12	0.043	348:	12	-0.058
43:			94:	10	0.009	145:	18	0.011	196:			247:	13	0.045	349:		
44:			95:	10	0.112	146:			197:			248:			350:		
45:			96:	10	-0.015	147:			198:			249:	12	-0.014	351:	27	-0.046
46:			97:			148:	9	-0.083	199:			250:	15	0.015	352:	15	0.006
47:			98:			149:	13	-0.058	200:			251:			353:	14	-0.014
48:			99:	18	0.006	150:	11	-0.026	201:			252:			354:	11	-0.049
49:			100:	18	0.018	151:			202:			253:	14	-0.016	355:	14	-0.048
50:			101:	10	0.106	152:	11	0.009	203:			254:	12	0.015	356:		
51:			102:	8	0.172	153:			204:			255:	10	0.032	357:		
52:			103:	13	-0.013	154:			205:			256:	9	0.027	358:		
53:			104:			155:	21	-0.037	206:			257:	14	-0.011	359:		
54:			105:			156:	10	-0.069	207:			258:			360:		
55:			106:	18	-0.069	157:	15	0.017	208:			259:			361:		
56:			107:	10	-0.045	158:	4	-0.051	209:			260:	17	-0.064	362:		
57:			108:	10	0.034	159:	8	0.009	210:			261:	9	-0.002	363:		

TABLE C-6.3. THE DAILY MEAN OF THE DIFFERENCES IN "PERCENTAGE DIFFERENCE FROM THE MEAN" WITH RESPECT TO THE *peak flow values* IN THE GROUP *CNSLD grade 2+3* (N IS THE NUMBER OF PAIRS IN WHICH THE DATA WERE AVAILABLE).

DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.	DAY	N	DIFF.
7:			59:			109:	4	0.045	160:			211:	1	0.012	262:	16	-0.032
8:			59:			110:	2	0.011	161:			212:	2	-0.017	263:	11	-0.026
9:			60:			111:			162:			213:	0	-0.046	264:	12	-0.001
10:			61:			112:			163:	21	-0.002	214:	3	0.029	265:		
11:			62:			113:			164:	10	0.138	215:	2	0.118	266:		
12:			63:			114:	1	0.152	165:	4	0.013	216:			267:	15	-0.020
13:			64:			115:	7	0.082	166:	6	0.057	217:			268:	9	-0.047
14:			65:			116:	5	0.235	167:			218:	10	-0.093	269:	18	-0.040
15:			66:			117:	8	-0.012	168:			219:	0	0.051	270:	11	-0.054
16:			67:			118:			169:	10	0.012	220:	12	0.001	271:	10	0.024
17:			68:			119:			170:	5	-0.058	221:	4	0.023	272:		
18:			69:			120:			171:	6	0.048	222:	8	-0.069	273:		
19:			70:			121:	2	-0.074	172:	3	-0.132	223:			274:	12	-0.018
20:			71:			122:	7	0.016	173:	3	0.057	224:			275:	7	0.143
21:			72:			123:	7	0.138	174:			225:	7	-0.023	276:	13	-0.028
22:			73:			124:	8	0.048	175:			226:	6	-0.035	277:	12	-0.015
23:			74:			125:			176:	8	0.056	227:	34	0.030	278:	10	0.036
24:			75:			126:			177:	6	-0.011	228:	8	0.008	279:		
25:			76:			127:	10	-0.003	178:	10	-0.017	229:	10	-0.011	280:		
26:			77:			128:	4	0.043	179:	6	0.030	230:			281:	10	0.038
27:			78:			129:	7	-0.076	180:	5	0.020	231:			282:	3	0.030
28:			79:			130:	8	0.135	181:			232:	8	-0.143	283:	16	-0.026
29:			80:			131:	10	-0.027	182:			233:	9	-0.065	284:	10	0.048
30:			81:			132:			183:			234:	13	-0.053	285:	11	-0.041
31:			82:			133:			184:			235:	10	-0.041	286:		
32:			83:			134:	37	-0.038	185:			236:	9	-0.072	287:		
33:			84:			135:	11	-0.019	186:			237:			288:	10	0.077
34:			85:			136:	14	0.082	187:			238:			289:	7	0.023
35:			86:			137:	5	0.049	188:			239:	13	-0.027	290:	12	0.024
36:			87:			138:	5	-0.007	189:			240:	7	-0.002	291:	7	0.016
37:			88:			139:			190:			241:	16	-0.092	292:	10	-0.032
38:			89:			140:			191:			242:	10	0.014	293:		
39:			90:			141:	11	0.026	192:			243:	14	-0.028	294:		
40:			91:			142:	9	0.038	193:			244:			295:	10	-0.047
41:			92:	5	0.043	143:	12	0.190	194:			245:			296:	7	0.126
42:			93:	2	0.110	144:	11	0.025	195:			246:	12	-0.081	297:	15	-0.011
43:			94:	6	0.029	145:	11	-0.042	196:			247:	5	-0.049	298:	10	-0.042
44:			95:	9	0.167	146:			197:			248:			299:	15	-0.094
45:			96:	5	0.006	147:			198:			249:	12	0.029	300:		
46:			97:			148:	11	-0.054	199:			250:	10	-0.031	301:		
47:			98:			149:	10	-0.084	200:			251:			302:	14	-0.007
48:			99:	10	-0.027	150:	14	0.034	201:			252:			303:	10	-0.018
49:			100:	2	0.203	151:			202:			253:	13	-0.011	304:	17	-0.095
50:			101:	8	0.079	152:	6	0.012	203:			254:	11	-0.042	305:	11	-0.026
51:			102:	6	0.144	153:			204:			255:	15	-0.076	306:	13	-0.030
52:			103:	7	0.021	154:			205:			256:	12	-0.012	307:		
53:			104:			155:	16	0.016	206:			257:	10	-0.022	308:		
54:			105:			156:	8	-0.040	207:			258:			309:	12	-0.010
55:			106:	6	-0.007	157:	12	0.036	208:			259:			310:	11	0.084
56:			107:	7	0.613	158:	10	-0.024	209:			260:	13	-0.058	311:	13	-0.033
57:			108:	8	0.084	159:	7	-0.009	210:			261:	8	-0.012	312:	10	0.025

TABLE D-1. THE 24-hour average CONCENTRATION OF sulphur dioxide IN VLAARDINGEN AND OMMOORD
DURING THE YEAR OF INVESTIGATION (IN MICROGRAMS/M³).

DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM
7:	148	114	53:	38	40	109:	15	20	160:	76	20	211:	13	0	262:	81	9
8:	79	143	54:	53	82	110:	14	63	161:	36		212:	13		263:	110	13
9:	116	77	55:	81	260	111:	28	47	162:	41		213:	49		264:	79	6
10:	169	114	56:	60	175	112:	36	39	163:	15	44	214:	51	3	265:	88	19
11:	152	100	57:	56	24	113:	28	32	164:	33	91	215:	95	62	266:	47	19
12:	150	83	58:	43	90	114:	31	23	165:	26	47	216:	101	22	267:	55	21
13:	180	76	59:	121	178	115:	21	13	166:	44	74	217:	228	4	268:	33	21
14:	166	65	60:	50	89	116:	143	92	167:	4	6	218:	189	11	269:	165	43
15:	148	34	61:	60		117:	79	81	168:	49	56	219:	95	19	270:	58	14
16:	203	83	62:	56	107	118:	48	25	169:	10	22	220:	63	21	271:	118	33
17:	112	44	63:	43	31	119:	34	30	170:	50	14	221:	173	22	272:	128	23
18:	72	29	64:	101	59	120:	57	42	171:	30	24	222:	44	48	273:	53	13
19:	156	63	65:	70	61	121:	66	41	172:	27	21	223:			274:	18	7
20:	174	68	66:	71	42	122:	52	32	173:			224:			275:	41	13
21:	125	36	67:	72	78	123:	46	15	174:			225:	34		276:	20	
22:	122	92	68:	73	118	124:	53	50	175:			226:	89	3	277:	164	20
23:	193	84	69:	74	98	125:	58	43	176:			227:	105	5	278:	155	24
24:	145	77	70:	160	110	126:	121	18	177:			228:	121	2	279:	107	12
25:	180	94	71:	111	43	127:	43	54	178:			229:	78	56	280:	116	27
26:	133	110	72:	77	35	128:	35	56	179:		9	230:			281:	62	27
27:	37	67	73:	78	64	129:	41	70	180:		32	231:	23		282:	74	32
28:	78	60	74:	79	89	130:	35	30	181:		31	232:	44	11	283:	100	35
29:	101	75	75:	80	248	131:	31	30	182:		8	233:	14		284:	27	20
30:	122	126	76:	81	279	132:	49	63	183:		16	234:	16		285:	96	52
31:	153	165	77:	82	327	133:	3	74	184:		34	235:	32		286:	85	43
32:	153	250	78:	83	166	134:	73	31	185:		9	236:	22		287:	88	42
33:	564	245	79:	84	138	135:	36	21	186:		10	237:	14		288:	43	48
34:	483	116	80:	85	153	136:	32	35	187:			238:	9		289:	87	27
35:	484	81	81:	86	208	137:	63	54	188:		13	239:	75		290:	51	32
36:	103	99	82:	87	193	138:	71	29	189:		10	240:	35		291:	56	29
37:	58	48	83:	88	51	139:	63	28	190:		10	241:	106		292:	44	26
38:	120	95	84:	89	115	140:	63	24	191:		45	242:	77	41	293:	41	26
39:	91	60	85:	90	164	141:	77	72	192:		28	243:	43	46	294:	18	14
40:	158	79	86:	91	105	142:	56	31	193:		6	244:	77	27	295:	111	48
41:	185	105	87:	92	113	143:		24	194:	35	23	245:	83	23	296:	24	15
42:	171	115	88:	93	62	144:	42	24	195:	39	8	246:	92	26	297:	148	64
43:	68	128	89:	94	200	145:	88	70	196:			247:	173	77	298:	133	91
44:	131	70	90:	95	81	146:	46	17	197:		14	248:	140	88	299:	187	92
45:	141	43	91:	96	81	147:	39	3	198:		20	249:	103	93	300:	130	55
46:	122	71	92:	97	41	148:	54	26	199:	43	16	250:	83	2	301:	122	89
47:	132	69	93:	98	89	149:	85	38	200:	69	23	251:	21		302:	72	46
48:	122	76	94:	99	11	150:	71	26	201:	61	36	252:	7		303:	60	50
49:	55	83	100:	100	99	151:	60	43	202:	47	23	253:	6		304:	101	24
50:	141	69	101:	101	56	152:	27	22	203:	85	17	254:	23		305:	131	64
51:	151	178	102:	102	46	153:		13	204:	44	19	255:	39	8	306:	221	103
52:	61	76	103:	103	73	154:	78	35	205:	46	24	256:	30		307:	148	52
53:	67	72	104:	104	111	155:	35	41	206:	46	20	257:	44	9	308:	99	38
54:	38	127	105:	105	61	156:	19	17	207:	6	4	258:	94	9	309:	93	39
55:	71	89	106:	106	26	157:	23		208:	6	5	259:	140	15	310:	35	24
56:	106	76	107:	107	49	158:	18		209:	5	0	260:	75	29	311:	126	32
57:	116		108:	108	31	159:	16		210:		1	261:	13	7	312:	126	53
															313:	84	76
															314:	34	30
															315:		26
															316:	41	46
															317:	52	
															318:	63	
															319:	69	
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															363:		

TABLE D-2. THE 24-hour average CONCENTRATION OF standard smoke IN VLAARDINGEN AND OMMOORD DURING THE YEAR OF INVESTIGATION (IN MICROGRAMS/M³).

DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM
7:	12	9	58:	19	45	109:	4	2	160:	9	12	211:	9	5	262:	11	12
8:	21	5	59:	13	38	110:	5	6	161:	5	5	212:	15		263:	21	24
9:	24	4	60:	17	19	111:	5	6	162:	4	5	213:	37	24	264:	14	15
10:	42	20	61:	13	15	112:	14	16	163:	19		214:	31	24	265:	7	6
11:	38	54	62:	9	11	113:	14	14	164:	7		215:	11	19	266:	10	9
12:	44	36	63:	7	38	114:	19	16	165:	5		216:	6	4	267:	23	17
13:	68	52	64:	7	21	115:	14	9	166:	22		217:	6	4	268:	11	21
14:	31	28	65:	5	12	116:	26	25	167:	8		218:	10	5	269:	22	49
15:	18	19	66:	5		117:	32	31	168:	13		219:	4	8	270:	11	12
16:	30	47	67:	15	18	118:	28	20	169:	7	7	220:	4	6	271:	7	10
17:	47	34	68:	9	8	119:	13	14	170:	17	17	221:	11	19	272:	4	4
18:	38	29	69:	11	20	120:	25	20	171:	17	18	222:	14	20	273:	3	2
19:	77	64	70:	2	6	121:	14	9	172:	16	11	223:	13	12	274:	13	6
20:	55	52	71:	7	5	122:	18	11	173:	6		224:	4	6	275:	16	13
21:	7	7	72:	17	17	123:	25	16	174:	4		225:	19	14	276:	16	
22:	20	22	73:	30	27	124:	17	15	175:	4		226:	33	24	277:	67	39
23:	29	35	74:	18	45	125:	19	8	176:	9		227:	38	22	278:	97	65
24:	38	38	75:	26	21	126:	2	2	177:	24		228:	50	36	279:	75	50
25:	47	53	76:	23	22	127:	5	7	178:	15		229:	56	69	280:	21	21
26:	30	35	77:	7	6	128:	6	8	179:	11		230:	10	10	281:	20	25
27:	7	5	78:	8	5	129:	7	9	180:	8		231:	17	13	282:	7	11
28:	5	10	79:	15	25	130:	3	5	181:	8		232:	16	21	283:	7	9
29:	24	19	80:	31	51	131:	7	5	182:	11		233:	8	4	284:	13	9
30:	20	30	81:	53	63	132:	5	7	183:	20		234:	9	5	285:	27	22
31:	26	27	82:	66	76	133:	3	4	184:	11		235:	27	18	286:	22	20
32:	46	71	83:	36	45	134:	23	7	185:	12		236:	20	15	287:	31	28
33:	59	89	84:	7	70	135:	13	6	186:	16		237:	8	5	288:	31	39
34:	24	27	85:	16	18	136:	8	5	187:	9		238:	9	2	289:	34	26
35:	22	20	86:	45	32	137:	16	10	188:	16		239:	44	19	290:	7	11
36:	39	46	87:	29	29	138:	31	17	189:	3		240:	27	22	291:	5	6
37:	31	23	88:	10	8	139:	27	22	190:	5		241:	23	20	292:	9	10
38:	38	13	89:	26	26	140:	11	5	191:	18		242:	7	14	293:	7	9
39:	23	15	90:	12	10	141:	24	22	192:	15		243:	8	7	294:	2	1
40:	17	16	91:	4	4	142:	9	11	193:	3		244:	4	7	295:	13	31
41:	22	10	92:	5	5	143:		10	194:	9	8	245:	4	4	296:	8	5
42:	20	19	93:	4	4	144:	12	6	195:	18	14	246:	5	9	297:	28	59
43:	10	14	94:	15	21	145:	25	22	196:		10	247:	39	40	298:	32	61
44:	8	10	95:	6	7	146:	22	14	197:		8	248:	53	34	299:	68	61
45:	11	17	96:	6	7	147:	9	5	198:		10	249:	30	27	300:	55	47
46:	5	23	97:	5	3	148:	16	14	199:	8	4	250:	44	51	301:	49	47
47:	14	21	98:	6	4	149:	6	12	200:	6	11	251:	27	19	302:	22	26
48:	14	16	99:	6	6	150:	8	14	201:	5	8	252:	10	9	303:	27	21
49:	17	14	100:	5	4	151:	5	8	202:	3	3	253:	5	5	304:	32	18
50:	35	7	101:	8	5	152:	7	8	203:	4	3	254:	11	8	305:	50	42
51:	34	12	102:	5	3	153:	4	3	204:	5	5	255:	25	16	306:	75	76
52:	16	5	103:	12	7	154:	4	5	205:	8	4	256:	13	6	307:	73	53
53:	13	5	104:	14	29	155:	7	10	206:	8	5	257:	26	20	308:	27	22
54:	5	7	105:	8	6	156:	9	4	207:	2	2	258:	28	18	309:	10	10
55:	6	36	106:	9	4	157:	9	5	208:	3	2	259:	13	14	310:	10	8
56:	13	11	107:	5	3	158:	10	5	209:	3	2	260:	24	30	311:	18	13
57:	39		108:	4	4	159:	8	4	210:	4	4	261:	10	19	312:	18	13

TABLE D-3. THE *daily average* CONCENTRATION OF *nitrogen monoxide* IN VLAARDINGEN AND OMMOORD
DURING THE YEAR OF INVESTIGATION (IN MICROGRAMS/M³).

DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM
7:			58:	60		109:	4	7	160:	8	15	211:	4		262:	43	9
8:			59:	19		110:	8	11	161:	8	11	212:	7		263:	34	20
9:			60:	15		111:	6	11	162:	13	11	213:	12		264:	31	13
10:			61:	14	30	112:	13	13	163:	13	23	214:	9		265:	16	10
11:			62:	12	10	113:	11	12	164:	13	10	215:	18		266:	23	14
12:			63:	11	7	114:	10	12	165:	79	10	216:	5		267:	76	17
13:			64:	17	9	115:	10	14	166:	34	29	217:	7		268:	59	48
14:			65:	13		116:	25	20	167:	25	15	218:	6		269:	49	61
15:		11	66:	11		117:	17	21	168:	25	16	219:	5		270:	25	13
16:	64	39	67:	16	0	118:	16	14	169:	21	13	220:	6		271:	21	7
17:	57	30	68:	31	6	119:	18	7	170:	38	17	221:	15		272:	14	6
18:	30	18	69:	63	12	120:	18	9	171:	28	25	222:	21		273:	20	5
19:	53	22	70:	17	21	121:	24	10	172:	25	13	223:	8		274:	14	
20:	48	30	71:	15	8	122:	18	10	173:	20	8	224:	7		275:	36	17
21:	24	6	72:	15	13	123:	19	13	174:	15	5	225:	9		276:	26	11
22:	26	19	73:	23	15	124:	16	16	175:	30	5	226:	11		277:	101	17
23:	43	30	74:	14	18	125:	19	15	176:	40	12	227:	12		278:	249	
24:	62	28	75:	66	25	126:	4	5	177:	40	16	228:	14		279:	174	
25:	56	28	76:	15	12	127:	6	1	178:	30	10	229:	22		280:	29	
26:	35	33	77:	6	5	128:	4	9	179:	8	8	230:	7		281:	35	
27:		14	78:	14	7	129:	6	10	180:	15	5	231:	7		282:	21	5
28:			79:	16	25	130:	4	15	181:	15	8	232:	10		283:	21	8
29:			80:		48	131:	5	17	182:		8	233:	6		284:	36	14
30:			81:		47	132:	6	12	183:		12	234:	18	6	285:	69	36
31:			82:	44	45	133:	4	3	184:		7	235:	27	8	286:	64	25
32:			83:	20	20	134:	7	1	185:		6	236:	30	7	287:	65	29
33:	62		84:	9	12	135:		13	186:		7	237:	23	6	288:	72	39
34:	38		85:	29	19	136:	7	10	187:		9	238:	20	5	289:	64	30
35:	42		86:	76	29	137:	11	12	188:		6	239:	48	12	290:	20	16
36:	34		87:	65	24	138:	23	16	189:		3	240:	37	9	291:	17	9
37:	22		88:	20	9	139:	17	15	190:		5	241:		8	292:	23	7
38:	15		89:	55	27	140:	20	12	191:		9	242:	60	12	293:	20	15
39:	11		90:	9	7	141:	30	24	192:		9	243:	14	5	294:	20	3
40:	15		91:	4	4	142:	30	16	193:		4	244:	10	5	295:	34	40
41:	10		92:	5	5	143:	23	14	194:		6	245:	11	5	296:	17	2
42:	10		93:	7	6	144:	15	8	195:		6	246:	19	14	297:	126	73
43:	8		94:	10	15	145:	30	16	196:		7	247:	61	28	298:	65	86
44:	14		95:	10	10	146:	28	13	197:		9	248:	79	17	299:	143	86
45:	17		96:	9	7	147:	15	13	198:		7	249:	22	13	300:	71	40
46:	45		97:	6	10	148:		15	199:		5	250:	75	23	301:	38	34
47:	51	13	98:	9	9	149:		16	200:		6	251:	50	12	302:	97	10
48:		15	99:	20	10	150:		14	201:		8	252:	16	5	303:	54	
49:		3	100:	12	9	151:		14	202:		4	253:		4	304:	61	
50:		12	101:	6	10	152:		10	203:		4	254:		8	305:	53	53
51:		40	102:	7	10	153:		6	204:		5	255:		15	306:	82	106
52:	22	12	103:	16	17	154:		9	205:		4	256:	87	7	307:	79	59
53:	15	6	104:	40	46	155:		10	206:		4	257:	45	13	308:	46	25
54:	8		105:	6	7	156:	8	9	207:		2	258:	38	9	309:	12	9
55:	8		106:	9	8	157:	8	12	208:		1	259:	26	18	310:	10	4
56:	36		107:	4	7	158:	8	11	209:		3	260:	45	38	311:	13	7
57:	112		108:	4	6	159:	8	8	210:		4	261:	27	18	312:	70	9

DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM
7:			54:	284		109:	7	17	160:	10	42	211:	9		262:	118	18
8:			59:	42		110:	28	28	161:	10	23	212:	12		263:	96	107
9:			60:	30		111:	18	32	162:	20	72	213:	26		264:	76	45
10:			61:	32	142	112:	29	38	163:	20	96	214:	17		265:	34	50
11:			62:	29	19	113:	48	26	164:	20	23	215:	74		266:	92	37
12:			63:	13	9	114:	23	25	165:	168	22	216:	6		267:	249	79
13:			64:	42	11	115:	30	26	166:	80	92	217:	14		268:	262	298
14:			65:	29		116:	55	31	167:	68	28	218:	22		269:	101	146
15:			66:	37		117:	34	46	168:	40	24	219:	6		270:	58	40
16:	104	82	67:	61	0	118:	59	37	169:	65	21	220:	30		271:	78	16
17:	128	49	68:	98	52	119:	131	14	170:	110	39	221:	101		272:	27	13
18:	57	37	69:	224	17	120:	65	9	171:	45	84	222:	119		273:	37	9
19:	73	38	70:	105	40	121:	104	19	172:	45	21	223:	10		274:		40
20:	75	46	71:	63	40	122:	48	25	173:	30	16	224:	11		275:	105	50
21:	51	23	72:	44	87	123:	58	34	174:	20	7	225:	14		276:	51	19
22:	40	47	73:	59	28	124:	41	34	175:	40	9	226:	21		277:	256	49
23:	83	57	74:	43	29	125:	46	35	176:	60	47	227:	10		278:	896	
24:	97	77	75:	265	72	126:	6	24	177:	60	55	228:	22		279:	875	
25:	101	47	76:	53	38	127:	12	1	178:	40	14	229:	63		280:	73	
26:	56	45	77:	9	9	128:	7	22	179:	10	11	230:	9		281:	110	
27:	20		78:	33	20	129:	11	26	180:	20	9	231:	13		282:	36	8
28:			79:	23	116	130:	10	32	181:	20	15	232:	30		283:	40	23
29:			80:		125	131:	9	36	182:		11	233:	8		284:	153	78
30:			81:		147	132:	10	31	183:		21	234:	20	10	285:	121	89
31:			82:	82	248	133:	6	15	184:		13	235:	60	11	286:	157	35
32:			83:	57	39	134:	22	1	185:		10	236:	70	9	287:	99	48
33:	73		84:	13	30	135:		125	186:		14	237:	50	9	288:	229	128
34:	48		85:	91	48	136:	13	23	187:		11	238:	63	8	289:	131	48
35:	68		86:	160	53	137:	20	26	188:		12	239:	153	36	290:	65	92
36:	58		87:	161	70	138:	70	30	189:		5	240:	75	16	291:	38	41
37:	34		88:	65	17	139:	28	25	190:		6	241:		15	292:	30	16
38:	22		89:	327	143	140:	104	19	191:		24	242:	66	41	293:	30	38
39:	18		90:	25	13	141:	40	90	192:		23	243:	28	13	294:	30	5
40:	26		91:	7	7	142:	40	28	193:		9	244:	18	4	295:	115	181
41:	17		92:	19	7	143:	35	26	194:		9	245:	18	7	296:	84	9
42:	14		93:	36	30	144:	20	23	195:		10	246:	29	52	297:	610	327
43:	12		94:	18	37	145:	50	26	196:		14	247:	298	54	298:	104	182
44:	64		95:	15	21	146:	45	26	197:		11	248:	323	31	299:	226	154
45:	44		96:	12	26	147:		29	198:		12	249:	35	32	300:	145	65
46:	112		97:	9	26	148:		25	199:		8	250:	170	78	301:	54	56
47:	183	36	98:	40	21	149:		26	200:		11	251:	104	28	302:	358	15
48:		73	99:	64	22	150:		23	201:		18	252:	47	10	303:	135	
49:		4	100:	48	23	151:		26	202:		7	253:		8	304:	120	
50:		33	101:	13	22	152:		20	203:		7	254:		31	305:	92	116
51:		88	102:	16	24	153:		16	204:		14	255:		60	306:	126	201
52:	48	28	103:	125	75	154:		21	205:		8	256:	142	12	307:	137	106
53:	24	10	104:	131	164	155:		28	206:		10	257:	95	39	308:	81	88
54:	12		105:	9	16	156:		18	207:		3	258:	82	15	309:	17	27
55:	16		106:	19	24	157:		10	208:		3	259:	62	63	310:	18	11
56:	148		107:	6	19	158:		10	209:		5	260:	109	104	311:	33	18
57:	387		108:	9	12	159:		10	210:		7	261:	26	55	312:	206	17

TABLE D-5. THE *daily average* CONCENTRATION OF *nitrogen dioxide* IN VLAARDINGEN AND OMMOORD
DURING THE YEAR OF INVESTIGATION (IN MICROGRAMS/M³).

DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM
7:			94:	45	50	109:	13	12	160:	28	36	211:	34	16	262:	44	32
8:			99:	37	53	110:	23	26	161:	21	24	212:	40	22	263:	54	35
9:			60:	35		111:	27	37	162:	26	26	213:	70	40	264:	44	35
10:			61:	26	39	112:	36	38	163:	42	51	214:	70	35	265:	31	26
11:			62:	21	40	113:	35	36	164:	28	27	215:	40	51	266:	41	34
12:		15	63:	22	48	114:	34	33	165:	38	24	216:	25	21	267:	63	43
13:		15	64:	35	67	115:	28	27	166:	59	51	217:	25	23	268:	44	35
14:			65:	27	36	116:	59	64	167:	43	25	218:	23	21	269:	67	66
15:			66:	24	26	117:	51	52	168:	45	41	219:	23	26	270:	41	39
16:		26	67:	31	36	118:	55	42	169:	33	27	220:	23	24	271:	37	35
17:	21		68:	39	33	119:	29		170:	50	36	221:	40	42	272:	34	28
18:	18		69:	46	45	120:	46		171:	52	44	222:	50	46	273:	30	20
19:	19		70:	26	21	121:	31		172:	40	42	223:	34	20	274:	49	
20:	19		71:	33	24	122:	31		173:	27	27	224:	24	18	275:	61	
21:	19		72:	36	24	123:	42		174:	23	13	225:	46	27	276:	41	
22:	20		73:	47	36	124:	49		175:	30	14	226:	56	36	277:	86	
23:	26		74:	35	36	125:			176:	49	25	227:	87	39	278:	107	33
24:	22		75:	52	45	126:			177:	81	47	228:	93	47	279:	92	28
25:	23		76:	41	45	127:			178:	49	31	229:	94	96	280:	92	
26:	23	32	77:	17	15	128:			179:	34	31	230:	30	16	281:	52	
27:		10	78:	32	29	129:			180:	26	29	231:	43	26	282:	36	21
28:		13	79:	45	53	130:			181:	40	37	232:	39	34	283:	38	24
29:		18	80:	50	76	131:			182:	61	30	233:	28	15	284:	49	22
30:		19	81:	78	63	132:			183:	67	37	234:	34	20	285:	74	32
31:		16	82:	100	101	133:			184:	35	34	235:	53	26	286:	65	29
32:		23	83:	56	76	134:			185:	56	20	236:	47	25	287:	53	24
33:		26	84:	28	45	135:		19	186:	42	24	237:	39	21	288:	58	32
34:		27	85:	44	58	136:		28	187:	40	33	238:	28	12	289:	53	22
35:		29	86:	60	56	137:		30	188:		20	239:	87	36	290:	37	20
36:		29	87:	44	63	138:		47	189:		10	240:	67	35	291:	36	21
37:		24	88:	32	34	139:		46	190:		20	241:	66	40	292:	38	26
38:		23	89:	36	50	140:		31	191:		36	242:	34	31	293:	55	26
39:		18	90:	28	44	141:		48	192:		35	243:	26	25	294:	45	11
40:		24	91:	15	30	142:		45	193:		13	244:	21	29	295:	63	36
41:		19	92:	16	21	143:		36	194:		27	245:	20	22	296:	29	14
42:		20	93:	16	19	144:		29	195:		36	246:	24	37	297:	78	47
43:		22	94:	35	57	145:		60	196:		33	247:	62	69	298:	71	55
44:			95:	22	45	146:		38	197:		28	248:	64	55	299:	106	53
45:			96:	19	31	147:		22	198:	33	31	249:	52	54	300:	47	
46:			97:	14	15	148:		43	199:	29	26	250:	89	62	301:	75	
47:		43	98:	25	27	149:		40	200:	27	31	251:	56	35	302:	61	
48:		30	99:	36	50	150:		34	201:	25	27	252:	34	17	303:	51	
49:		18	100:	27	22	151:		41	202:	18		253:	41	16	304:	66	
50:		45	101:	17	16	152:		25	203:	19		254:	55	30	305:	72	55
51:		51	102:	19	20	153:		20	204:	28	30	255:	61	36	306:	81	55
52:		32	103:	45	35	154:		34	205:	33	19	256:	44	24	307:	89	52
53:		26	104:	83	59	155:		34	206:	28	19	257:	61	42	308:	61	45
54:		14	105:		26	156:		20	207:	14	7	258:	83	43	309:	37	47
55:		18	106:		22	157:		24	208:	14	8	259:	50	40	310:	29	17
56:		38	107:	104	16	158:	24	17	209:	15	11	260:	70	52	311:	36	23
57:		56	108:	38	12	159:	21	16	210:	18	21	261:	41	36	312:	44	32

TABLE D-6. THE *daily maximum* CONCENTRATION OF *nitrogen dioxide* IN VLAARDINGEN AND OMMOORD DURING THE YEAR OF INVESTIGATION (IN MICROGRAMS/M³).

DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM
7:			53:	74	60	109:	20	18	160:	48	80	211:	54	44	262:	79	51
8:			59:	44	70	110:	47	61	161:	31	61	212:	90	58	263:	94	61
9:			60:	53		111:	61	66	162:	56	77	213:	126	58	264:	73	57
10:			61:	49	65	112:	59	74	163:	72	94	214:	120	88	265:	63	57
11:			62:	38	57	113:	80	72	164:	72	79	215:	100	126	266:	76	52
12:		20	63:	35	66	114:	66	71	165:	85	72	216:	37	43	267:	84	60
13:		20	64:	49	91	115:	56	42	166:	111	150	217:	45	38	268:	89	75
14:			65:	46	67	116:	119	130	167:	67	63	218:	33	43	269:	137	94
15:			66:	54	72	117:	95	113	168:	85	95	219:	29	56	270:	73	69
16:	31		67:	42	71	118:	68	63	169:	74	50	220:	55	79	271:	83	61
17:	35		68:	61	58	119:	64		170:	76	51	221:	92	86	272:	42	54
18:	22		69:	77	63	120:	76		171:	93	76	222:	80	109	273:	52	34
19:	23		70:	68	60	121:	56		172:	52	76	223:	59	33	274:	85	
20:	25		71:	57	40	122:	58		173:	42	55	224:	52	44	275:	80	
21:	25		72:	71	54	123:	76		174:	43	21	225:	87	56	276:	60	
22:	29		73:	75	51	124:	118		175:	69	44	226:	105	55	277:	123	
23:	31		74:	54	54	125:			176:	89	56	227:	114	60	278:	208	50
24:	30		75:	79	77	126:			177:	135	98	228:	178	99	279:	131	53
25:	28		76:	80	73	127:			178:	80	58	229:	180	227	280:	97	
26:	27	47	77:	41	35	128:			179:	78	53	230:	55	24	281:	78	
27:	18		78:	70	73	129:			180:	48	47	231:	78	67	282:	46	29
28:	31		79:	74	83	130:			181:	81	70	232:	68	94	283:	52	38
29:	26		80:	94	103	131:			182:	161	63	233:	58	30	284:	84	46
30:	26		81:	144	121	132:			183:	149	80	234:	55	36	285:	110	53
31:	24		82:	163	151	133:			184:	60	68	235:	80	41	286:	80	38
32:	64		83:	137	130	134:			185:	142	58	236:	76	46	287:	70	30
33:	55		84:	63	83	135:		37	186:	66	38	237:	73	43	288:	85	48
34:	32		85:	83	84	136:		49	187:	69	60	238:	73	28	289:	65	34
35:	33		86:	77	77	137:		43	188:	55	55	239:	165	64	290:	61	47
36:	32		87:	62	166	138:		65	189:	25	25	240:	93	65	291:	64	43
37:	30	35	88:	54	62	139:		61	190:	33	33	241:	108	76	292:	44	37
38:	33	35	89:	71	119	140:		74	191:	55	55	242:	49	61	293:	60	42
39:	25	35	90:	56	88	141:		99	192:	64	64	243:	49	58	294:	70	28
40:	45		91:	29	47	142:		60	193:	37	37	244:	32	50	295:	105	59
41:	31		92:	35	32	143:		49	194:	59	59	245:	29	41	296:	61	30
42:	32		93:	53	68	144:		69	195:	54	54	246:	38	53	247:	179	73
43:	26		94:	50	73	145:		82	196:	58	58	247:	108	168	248:	86	68
44:			95:	34	79	146:		65	197:	54	54	248:	120	125	249:	150	72
45:			96:	31	78	147:		45	198:	64	62	249:	103	86	300:	125	
46:			97:	27	27	148:		58	199:	51	52	250:	184	137	301:	98	
47:		68	98:	44	50	149:		61	200:	41	43	251:	98	68	302:	92	
48:		72	99:	63	54	150:		63	201:	85	32	252:	56	35	303:	78	
49:		36	100:	56	51	151:		63	202:	40		253:	61	44	304:	74	
50:		62	101:	31	33	152:		45	203:	35		254:	91	54	305:	103	60
51:		58	102:	43	57	153:		43	204:	67	42	255:	132	63	306:	122	72
52:		50	103:	42	70	154:		68	205:	98	54	256:	62	48	307:	113	59
53:		34	104:	111	76	155:		60	206:	86	66	257:	93	71	308:	85	60
54:		22	105:		60	156:		41	207:	21	9	258:	180	82	309:	53	64
55:		38	106:		58	157:		45	208:	23	16	259:	114	62	310:	41	31
56:		57	107:	218	34	158:		31	209:	23	40	260:	121	73	311:	62	37
57:	111	110	108:	90	16	159:	58	39	210:	38	36	261:	113	58	312:	67	50

TABLE D-7. THE *daily average* CONCENTRATION OF *ozone* IN VLAARDINGEN AND OMMOORD
DURING THE YEAR OF INVESTIGATION (IN MICROGRAMS/M³).

DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM
7:			58:			109:	49	65	160:	59	48	211:			262:	31	25
8:			59:			110:	37	56	161:	33	68	212:			263:	37	
9:			60:			111:	32	47	162:	44	41	213:			264:	39	
10:			61:			112:	29	42	163:	65	52	214:			265:	41	
11:			62:			113:	24	45	164:	55	62	215:			266:	34	
12:			63:		33	114:	53	44	165:	35	59	216:			267:	21	
13:			64:	20	27	115:	40	52	166:		50	217:			268:	48	
14:			65:	25	35	116:	45	57	167:		39	218:			269:	42	
15:			66:	25	45	117:	55	69	168:	117	66	219:			270:	37	50
16:			67:	20	43	118:	40	36	169:	43	69	220:			271:		
17:			68:	30	45	119:	55	52	170:	103	68	221:			272:		
18:			69:	20	40	120:	30		171:	100	50	222:			273:		
19:			70:	30	30	121:	35	35	172:	90	53	223:			274:		
20:			71:	25	35	122:	35	30	173:	117	69	224:			275:		
21:			72:	20		123:	38	21	174:	90	88	225:			276:		20
22:			73:	25	45	124:	13	37	175:	85	75	226:			277:		20
23:			74:	20	35	125:	14	40	176:	80	78	227:			278:		20
24:			75:	20	48	126:	14	73	177:	127	112	228:			279:		45
25:			76:	22	35	127:	22	57	178:	110	88	229:			280:		55
26:			77:	32	55	128:	42	52	179:	85	82	230:			281:		30
27:			78:	15	45	129:	34	54	180:	88	59	231:			282:		25
28:	2		79:	12	40	130:	52	72	181:	85	89	232:	90	20	283:		30
29:	3		80:	10	33	131:	53	58	182:			233:	53	20	284:		25
30:	8		81:	25	65	132:	46	66	183:			234:	70	20	285:		20
31:	5		82:	51	95	133:	52	68	184:			235:	80	20	286:		20
32:	7		83:	40	75	134:	34	47	185:			236:	93	20	287:		20
33:	15		84:	25	40	135:	34	38	186:			237:	60	20	288:		
34:	14		85:	27	40	136:	33	44	187:			238:	55	20	289:		
35:	13		86:	19	25	137:	59	72	188:			239:	110	25	290:		
36:	8		87:	31	50	138:	25	52	189:			240:	55	20	291:		
37:	16		88:	26	40	139:		51	190:			241:	70		292:	40	
38:	13		89:	38	60	140:		61	191:			242:	50	25	293:	43	20
39:	21		90:	45	60	141:	55	38	192:			243:	55	20	294:	40	20
40:	28		91:	43	49	142:	55	40	193:			244:	61	20	295:	37	25
41:			92:	46	55	143:	58	53	194:			245:	49	43	296:	43	55
42:			93:	55	60	144:	60	77	195:			246:	36	30	297:	60	55
43:			94:	39	33	145:		80	196:			247:	67	25	298:	25	55
44:			95:	32	36	146:	60	45	197:			248:	128	53	299:	35	50
45:			96:	44	53	147:	55	65	198:			249:	88	35	300:	38	50
46:			97:	50	65	148:	45	59	199:			250:	72	20	301:	49	20
47:	10		98:	36	46	149:	45	39	200:			251:	53	28	302:	38	20
48:	21		99:	27	45	150:	45	33	201:			252:	49	35	303:	28	20
49:	19		100:	36	57	151:		23	202:			253:	43	20	304:	23	50
50:	20		101:	39	54	152:	33	44	203:			254:	29	80	305:	29	23
51:	17		102:	41	55	153:	63	72	204:			255:	30	40	306:	24	50
52:	13		103:	30	44	154:	44	56	205:			256:	39	40	307:	31	50
53:	16		104:	25	33	155:		66	206:			257:	45	25	308:	31	50
54:			105:	35	51	156:	20	67	207:			258:	49	25	309:	35	20
55:			106:	30	46	157:	60	53	208:			259:	49	25	310:	47	20
56:			107:	42	65	158:	47	72	209:			260:	48	38	311:	36	20
57:			108:	44	64	159:	43	47	210:			261:	40	20	312:	30	50

TABLE D-8. THE *daily maximum* CONCENTRATION OF *ozone* IN VLAARDINGEN AND OMMOORD
DURING THE YEAR OF INVESTIGATION (IN MICROGRAMS/M³).

DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM
7:			93:			109:	65	73	160:	153	117	211:	262:	61	39	313:	60
8:			94:			110:	56	88	161:	75	192	212:	263:	84		314:	49
9:			95:			111:	61	72	162:	72	82	213:	264:	71		315:	69
10:			96:			112:	55	92	163:	105	124	214:	265:	64		316:	
11:			97:			113:	68	78	164:	75	125	215:	266:	70		317:	65
12:			98:			114:	75	90	165:	45	92	216:	267:	57		318:	65
13:			99:		33	115:	65	87	166:		139	217:	268:	62		319:	
14:			100:	25	93	116:	65	105	167:		72	218:	269:	52		320:	75
15:			101:	35	44	117:	85	117	168:	200	144	219:	270:	69		321:	
16:			102:	35	54	118:	55	80	169:	75	149	220:	271:			322:	
17:			103:	25	65	119:	85	95	170:	230	193	221:	272:			323:	
18:			104:	45	25	120:	45		171:	165	107	222:	273:			324:	
19:			105:	25	65	121:	55	51	172:	145	124	223:	274:			325:	
20:			106:	45	45	122:	55	55	173:	200	94	224:	275:			326:	
21:			107:	35	55	123:	50	41	174:	135	110	225:	276:			327:	25
22:			108:	35	65	124:	16	101	175:	135	128	226:	277:			328:	25
23:			109:	33	55	125:	18	86	176:	145	144	227:	278:			329:	25
24:			110:	38	70	126:	17	92	177:	325	184	228:	279:			330:	65
25:			111:	37	45	127:	60	91	178:	185	191	229:	280:			331:	75
26:			112:	40	75	128:	67	116	179:	125	103	230:	281:			332:	45
27:			113:	43	75	129:	60	109	180:	115	110	231:	282:			333:	35
28:	5		114:	21	65	130:	82	129	181:	155	160	232:	283:	135	25	334:	45
29:	6		115:	22	90	131:	75	104	182:			233:	284:	85	25	335:	35
30:	18		116:	47	115	132:	75	132	183:			234:	285:	125	25	336:	25
31:	4		117:	121	165	133:	76	106	184:			235:	286:	145	25	337:	25
32:	12		118:	83	72	134:	62	76	185:			236:	287:	160	25	338:	
33:	25		119:	84	34	135:	69	81	186:			237:	288:	105	25	339:	
34:	21		120:	85	44	136:	48	81	187:			238:	289:	95	25	340:	
35:	28		121:	86	32	137:	95	106	188:			239:	290:	195	35	341:	
36:	15		122:	87	70	138:	35	115	189:			240:	291:	95	25	342:	
37:	20		123:	88	47	139:		79	190:			241:	292:	120		343:	
38:	22		124:	89	77	140:		114	191:			242:	293:	65	35	344:	25
39:	36		125:	90	62	141:	85	77	192:			243:	294:	95	25	345:	25
40:	36		126:	91	55	142:	85	95	193:			244:	295:	95	25	346:	35
41:			127:	92:	61	143:	90	77	194:			245:	296:	73	65	347:	45
42:			128:	93:	64	144:	95	123	195:			246:	297:	51	45	348:	60
43:			129:	94:	64	145:		228	196:			247:	298:	246	35	349:	65
44:			130:	95:	46	146:	105	98	197:			248:	299:	343	90	350:	65
45:			131:	96:	71	147:	95	126	198:			249:	300:	158	50	351:	65
46:			132:	97:	66	148:	75	113	199:			250:	301:	159	25	352:	25
47:	34		133:	98:	55	149:	65	90	200:			251:	302:	181	40	353:	25
48:	68		134:	99:	55	150:	65	71	201:			252:	303:	100	55	354:	25
49:	25		135:	100:	57	151:		51	202:			253:	304:	77	25	355:	45
50:	35		136:	101:	51	152:	49	67	203:			254:	305:	76	145	356:	36
51:	23		137:	102:	60	153:	84	98	204:			255:	306:	86	55	357:	45
52:	16		138:	103:	44	154:	49	94	205:			256:	307:	64	65	358:	45
53:	56		139:	104:	52	155:		120	206:			257:	308:	137	35	359:	25
54:			140:	105:	51	156:	74	86	207:			258:	309:	114	35	360:	35
55:			141:	106:	46	157:	102	88	208:			259:	310:	85	35	361:	25
56:			142:	107:	53	158:	88	101	209:			260:	311:	141	50	362:	25
57:			143:	108:	56	159:	74	82	210:			261:	312:	64	25	363:	45

209

DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	
7:			58:	44	83	109:	35	60	160:	59	64	211:		3	88	313:	26	26
8:			59:	27	66	110:	25	40	161:	48	42	212:		138		314:	26	26
9:			60:	49	65	111:	24	59	162:	37	46	213:		91		315:	26	14
10:			61:	22	46	112:	31		163:	60	226	214:		90		316:	30	19
11:			62:	15	51	113:	35	84	164:	34	196	215:	54			317:	20	23
12:			63:	19	59	114:	25	26	165:	60	198	216:	45			318:	21	33
13:			64:	32	69	115:			166:	72	212	217:	72			319:	11	19
14:			65:	18	60	116:		75	167:	69	239	218:	83			320:	11	34
15:			66:	18	31	117:	189	90	168:	84	251	219:	30	47		321:	11	23
16:			67:	35	49	118:	43	82	169:		228	220:	36	47		322:	25	66
17:			68:	41	67	119:	50	57	170:	67		221:	68	84		323:	13	32
18:			69:	58	69	120:	47	57	171:			222:	56	126		324:	32	15
19:	33		70:	26	66	121:	31	49	172:	60		223:	67	154		325:	54	57
20:	79		71:	21	61	122:	40		173:	56		224:	56	146		326:	44	
21:	44		72:	20	62	123:	49	80	174:	64		225:	60	145		327:	21	
22:	50		73:	26	46	124:	42	79	175:	64		226:	75	157		328:	13	
23:	43		74:	22	52	125:	36	81	176:	87		227:	79	179		329:	21	
24:	43		75:	35	45	126:	24	14	177:	166		228:	112	164		330:	42	
25:	46		76:	24	38	127:	21		178:	79		229:	139	176		331:	14	
26:			77:	10	24	128:	33	46	179:			230:	70	134		332:	25	26
27:			78:	18	26	129:	35	43	180:	89		231:	97	136		333:	47	44
28:			79:	30	49	130:	35	45	181:	188		232:	89	96		334:	27	40
29:	74	35	80:	67	83	131:	39	59	182:	62		233:	38	116		335:	38	
30:	17	27	81:	117	86	132:	34	40	183:	67		234:		99		336:	33	62
31:	31	28	82:	127	126	133:	64	35	184:	96	82	235:	106			337:	34	22
32:	15	52	83:	54	65	134:	82	43	185:	89	93	236:		98		338:	19	25
33:	29	78	84:	35	61	135:	30	55	186:		79	237:		102		339:	13	25
34:	35	66	85:	31	66	136:	57		187:	81	39	238:		24		340:	30	25
35:	51	74	86:	55		137:	65	61	188:	53	37	239:		27		341:	32	36
36:		48	87:	66		138:	71	41	189:	46	50	240:		79		342:	46	47
37:	13	32	88:	31		139:	74		190:	45	20	241:		14		343:	36	40
38:	13	17	89:	35		140:	52	85	191:	67	86	242:		67		344:	34	42
39:	13	13	90:	20		141:	84	44	192:	97	73	243:		85		345:	27	49
40:	67	42	91:	22		142:	39	113	193:	32	87	244:		96		346:	24	53
41:	30	20	92:	32		143:		57	194:		97	245:		74		347:	16	24
42:	13	31	93:	16	68	144:	64	48	195:		119	246:		24		348:	26	24
43:	11	26	94:	30	49	145:	95	113	196:		116	247:		116		349:	13	27
44:	12	112	95:	27	35	146:	109	111	197:		109	248:		122		350:	17	32
45:	52	38	96:	32	48	147:	62	99	198:		92	249:	65	91		351:	28	23
46:	69	43	97:	14	35	148:	58	131	199:		56	250:	61	123		352:		38
47:	48	83	98:	23	77	149:	36	107	200:		100	251:	55	117		353:	16	95
48:	38	35	99:	76	97	150:	65	51	201:	33	82	252:	52	95		354:	36	64
49:	62	21	100:	46	178	151:	65	82	202:	39	68	253:	19	72		355:		72
50:	28	35	101:	28	82	152:	59	85	203:	47	62	254:	17	65		356:		76
51:	41	65	102:	29		153:	41	7	204:	41	54	255:	25	108		357:	1	65
52:	31	35	103:	27		154:	46	66	205:	98		256:	69	120		358:	43	84
53:	16	26	104:	44	94	155:	60	93	206:	52		257:	87	131		359:	37	91
54:	9	23	105:	16	75	156:	35	102	207:			258:	65	155		360:	31	51
55:	7	28	106:	31	57	157:	35	64	208:			259:	63	149		361:		55
56:	29	49	107:	44	45	158:	48	32	209:			260:	57	151		362:		51
57:	55	60	108:	22	48	159:	59	48	210:			261:	15	86		363:		

TABLE D-10. THE 8-hour average CONCENTRATION OF aldehydes IN VLAARDINGEN AND OMMOORD
DURING THE YEAR OF INVESTIGATION (IN MICROGRAMS/M³).

DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM
7:			58:	72	146	109:	53	78	160:	105	153	211:	111		262:		181	313:	30	46
8:			59:	82	86	110:	83	65	161:	53	69	212:	123		263:	91	367	314:	83	35
9:			60:	100	102	111:	47	66	162:	49	114	213:	144		264:	28	194	315:	33	32
10:			61:	35	175	112:	60	96	163:	93	275	214:	175		265:	63	151	316:	36	42
11:			62:	32	63	113:	59	86	164:	60	238	215:	102		266:	75	98	317:	28	25
12:			63:	22	79	114:	58	110	165:	123	176	216:	107		267:	88		318:	10	27
13:		71	64:	42	127	115:		101	166:	153	355	217:	105		268:	43	13	319:	15	26
14:	62		65:	22	98	116:		111	167:	129	524	218:	106		269:	83	149	320:	14	27
15:	88		66:	34	30	117:	249	89	168:	191	497	219:	59	57	270:		70	321:	23	26
16:	71		67:	43	62	118:	83	108	169:	104	573	220:	42	64	271:	48	206	322:	35	53
17:	62		68:	44	57	119:	75	105	170:	125		221:	111	171	272:	55	126	323:	11	20
18:	45		69:	80	77	120:	84	108	171:	138		222:	115	199	273:	36	156	324:	50	24
19:	158		70:	33	60	121:	39	62	172:	149		223:	111	262	274:	59	318	325:	58	86
20:	45		71:	31	67	122:	47		173:	104	577	224:	42	333	275:	35	321	326:	92	142
21:	65	112	72:	20	93	123:	68	109	174:	109	602	225:	174	289	276:	31	20	327:	30	43
22:	76	125	73:	37	222	124:	57	84	175:	107	474	226:	130	399	277:	128	56	328:	28	35
23:	83	208	74:	29	44	125:	65	93	176:	112	453	227:	129	210	278:	173	109	329:	25	6
24:	84	93	75:	44	91	126:	12	52	177:	344		228:	180	240	279:	130	64	330:	22	
25:	55	86	76:	29	18	127:	9	67	178:	119		229:	210	367	280:	62	35	331:	14	27
26:	57	92	77:		37	128:	15	100	179:	140		230:	121	178	281:	54	26	332:	20	36
27:	64	49	78:	109		129:	47		180:	206		231:	155	150	282:	33	83	333:	51	20
28:	53	45	79:	43	61	130:	69		181:	164		232:	123	148	283:	41	36	334:	40	28
29:	57	49	80:	57	88	131:	51		182:	219		233:	47	118	284:	54	25	335:	54	59
30:	38	56	81:	143	107	132:	82		183:	184		234:	75	179	285:	95	44	336:	100	31
31:	32	65	82:	255	139	133:	87		184:	121		235:	109	160	286:	69	44	337:	42	46
32:	55	119	83:	123	115	134:	155		185:	320		236:	100	163	287:	75	54	338:	20	69
33:	58	187	84:	45	59	135:	65		186:	161		237:	83	171	288:	109	60	339:	24	46
34:	48	92	85:	65	111	136:	102	268	187:	156		238:	91		289:	54	101	340:	45	36
35:	132	114	86:	106	107	137:	88	109	188:	344		239:	148		290:	40	44	341:	34	16
36:	73	91	87:	162	143	138:	113	105	189:	59		240:	120		291:	36	59	342:	54	21
37:	36	76	88:	48	60	139:	105	110	190:	100		241:	129	128	292:	40	44	343:	53	67
38:	19	37	89:	82	120	140:	68	83	191:	120	156	242:	86	113	293:	13	68	344:	54	27
39:	19	32	90:	31	44	141:	209	113	192:	85	151	243:	80	68	294:	17	40	345:	34	30
40:	25	44	91:	26	44	142:	64	178	193:	83	243	244:	66	112	295:	38	7	346:	43	66
41:	13	31	92:	24	56	143:	69	118	194:	123	161	245:	75	79	296:	16	30	347:	61	45
42:	14	68	93:	44	49	144:	98	99	195:	127	326	246:	75	182	297:	91	55	348:	115	31
43:	24	26	94:	51	45	145:	160	180	196:	100	311	247:	333	295	298:		81	349:	67	39
44:	20	50	95:	44	31	146:	124	109	197:	67	349	248:	403	269	299:	123	91	350:	46	29
45:		58	96:	56	43	147:	124	118	198:	91	180	249:	127	220	300:	112	60	351:	157	36
46:		226	97:	36	43	148:	124	152	199:	66		250:	207	243	301:	100	62	352:	35	56
47:	43	127	98:	35	58	149:	61	194	200:	77		251:	129	202	302:	70	36	353:	36	64
48:	43	71	99:	51	78	150:	63	105	201:	74		252:	104	127	303:	35	22	354:	102	38
49:	17	52	100:	42	99	151:	67	111	202:	67		253:	84	112	304:	31	69	355:	127	50
50:	13	28	101:	21	15	152:	94	155	203:	170		254:	109	129	305:	92		356:	116	31
51:	54	65	102:	18	4	153:	65	89	204:	159		255:	83		306:	89		357:	113	40
52:	18	37	103:	12	12	154:	94	111	205:	186		256:	52		307:	9	155	358:	83	59
53:		44	104:	25	51	155:	69	144	206:	41		257:	59	281	308:	84	160	359:	89	36
54:		25	105:	12	15	156:	61	187	207:	145		258:	69	312	309:	44	115	360:	56	37
55:		44	106:	72	13	157:		123	208:	92		259:	60	335	310:	40	55	361:	84	22
56:	34	61	107:	38	66	158:	110	114	209:	105		260:	4	397	311:	24	42	362:		20
57:	79	79	108:	59	57	159:	89	80	210:	84		261:	14	117	312:		58	363:		

TABLE E-1. THE *maximum temperature* IN VLAARDINGEN AND OMMOORD DURING THE YEAR OF INVESTIGATION
(IN CENTIGRADES X 10).

DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM
7:			58:	59	55	109:	101	96	160:	170	252	211:	190	191	262:	165		313:	127	114
8:			59:	47	37	110:	83	100	161:	218	179	212:	228	236	263:	200		314:	120	121
9:			60:	62	55	111:	86	92	162:	160	220	213:	267	282	264:	164	183	315:	110	100
10:			61:	69	61	112:	99	141	163:	238	257	214:	271	289	265:	175	153	316:	122	131
11:			62:	76	65	113:	91	115	164:	202	216	215:	213	207	266:	154	135	317:	126	133
12:			63:	82	68	114:	121	154	165:	173	174	216:	212	211	267:	173	131	318:	105	85
13:			64:	91	47	115:	154	160	166:	224	233	217:	194	194	268:	197	167	319:	110	91
14:			65:	72	41	116:	151	151	167:	258	272	218:	219	274	269:	175	165	320:	117	91
15:			66:	70	68	117:	153	155	168:	239	272	219:	196	188	270:	191	167	321:	80	91
16:			67:	95	102	118:	124	125	169:	238	251	220:	210	204	271:	189	172	322:	64	46
17:			68:	59	79	119:	134	135	170:	258	297	221:	226	228	272:	149	125	323:	112	114
18:			69:	45	99	120:	159	176	171:	239	271	222:	262	270	273:	152	138	324:	103	51
19:			70:	68	86	121:	159	115	172:	230		223:	271	284	274:	175	159	325:	94	81
20:			71:	66	67	122:	125		173:	236		224:	255	267	275:	181		326:	76	98
21:			72:	57	54	123:	189	194	174:	142		225:	289	295	276:	177	150	327:	108	100
22:			73:	70	73	124:	172	182	175:	249		226:	292	305	277:	210	185	328:	119	129
23:			74:	94	107	125:	201	217	176:	271	313	227:	288	303	278:	231	227	329:	81	64
24:			75:	91	96	126:	142		177:	291	351	228:	315	333	279:	222	200	330:	60	42
25:			76:	82	84	127:	157		178:	282	313	229:	278	292	280:	152	142	331:	54	31
26:			77:	87	91	128:	132		179:	227	251	230:	231	236	281:	171	151	332:	59	80
27:			78:	83		129:	162	160	180:	217	240	231:	249	258	282:	183	155	333:	41	14
28:			79:	113		130:	138	131	181:	242	279	232:		252	283:	166	149	334:	34	2
29:			80:	98	101	131:	128	128	182:	291	342	233:	206		284:	129	95	335:		20
30:			81:	142	149	132:		163	183:	300	359	234:	213	219	285:	111	80	336:		8
31:			82:	163	179	133:	143	142	184:	238	251	235:	250	262	286:	100	71	337:		66
32:			83:	184	201	134:	134	122	185:	240	262	236:	221	216	287:	114	92	338:	100	100
33:			84:	105	106	135:	144	238	186:	311	344	237:	227	241	288:	125	109	339:	94	41
34:			85:	135	117	136:	111	168	187:	263	283	238:	226	238	289:	115	105	340:	94	41
35:			86:	90	96	137:	193	196	188:	210	218	239:	272	284	290:	121	94	341:	104	95
36:			87:	114		138:	208	219	189:	201	209	240:	230	236	291:	103	75	342:	103	104
37:			88:	100		139:	207	208	190:		227	241:	216	226	292:	129	112	343:	57	30
38:			89:	124		140:	208	239	191:		262	242:	180	197	293:	134	130	344:	10	10
39:			90:	113		141:	230	251	192:		212	243:	201	199	294:	137	134	345:	47	40
40:			91:	82		142:	211	126	193:		229	244:	212	221	295:	122	113	346:	78	115
41:		39	92:			143:	176	186	194:		254	245:	206	221	296:	140	120	347:	64	65
42:		51	93:			144:	151	161	195:		263	246:	236	242	297:	153	130	348:	63	62
43:			94:		87	145:	207	213	196:		208	247:	261	278	298:	136	115	349:	60	53
44:	41	25	95:		107	146:	230	250	197:		230	248:	302	324	299:	150	124	350:	85	62
45:	37	21	96:		100	147:	243	261	198:	199	210	249:	231	250	300:	161	135	351:	62	50
46:	51	41	97:		78	148:	240	274	199:	200	214	250:	255	267	301:	141	118	352:	67	35
47:	32	30	98:		72	149:	191	195	200:	202	216	251:	244	268	302:	137	112	353:	41	27
48:		47	99:		68	150:	182	201	201:	210	223	252:	217	239	303:	148	115	354:	94	92
49:		41	100:		62	151:	181	192	202:	215	225	253:	203	189	304:	136	117	355:		125
50:		57	101:		67	152:	150	158	203:	197	201	254:	198		305:	122	110	356:		130
51:		83	102:		61	153:	151	155	204:	201	204	255:	191		306:	113	100	357:		66
52:		78	103:		77	154:	167	184	205:	202	197	256:	188		307:	159	144	358:		57
53:	94	62	104:		92	155:		199	206:	189	180	257:	220		308:	145	128	359:		
54:	51	40	105:	96	49	156:		236	207:	162	155	258:	255		309:		132	360:		70
55:	43	48	106:	97	123	157:	168	223	208:	164	153	259:	237		310:	96		361:	64	88
56:	23	26	107:	142	45	158:	191	224	209:	203	209	260:	251		311:	105	87	362:	40	
57:	47	47	108:	104	91	159:	209	193	210:	191	190	261:	179		312:	143	135	363:	73	

TABLE E-2. THE *minimum temperature* IN VLAARDINGEN AND OMMOORD DURING THE YEAR OF INVESTIGATION
(IN CENTIGRADES X 10).

DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM		
7:			58:	-42	-48	109:	66	15	160:	128	118	211:	151	139	262:	134	313:	111	101
8:			59:	0	-19	110:	57	23	161:	110	145	212:	150	130	263:	120	314:	99	81
9:			60:	20	7	111:	37	17	162:	130	131	213:	141	129	264:	124	315:	62	65
10:			61:	18	-1	112:	9	14	163:	130	128	214:	153	154	265:	102	316:	67	51
11:			62:	38	29	113:	61	24	164:	105	104	215:	161	158	266:	80	317:	69	64
12:			63:	54	46	114:	71	63	165:	94	90	216:	158	146	267:	60	318:	74	37
13:			64:	40	43	115:	38	23	166:	80	122	217:	137	120	268:	100	319:	64	33
14:			65:	20	12	116:	38	27	167:	130	131	218:	151	146	269:	89	320:	55	32
15:			66:	6	18	117:	55	49	168:	151	148	219:	130	112	270:	122	321:	41	25
16:			67:	-8	24	118:	50	50	169:	133	137	220:	146	138	271:	127	322:	26	5
17:			68:	16	2	119:	27	28	170:	118	190	221:	144	136	272:	90	323:	74	14
18:			69:	-30	-22	120:	23	11	171:	151		222:	152	147	273:	100	324:	42	47
19:			70:	-7	11	121:	63	48	172:	145		223:	150	150	274:	96	325:	20	15
20:			71:	-1	5	122:	30	39	173:	130		224:	138	130	275:	74	326:	11	2
21:			72:	-10	-14	123:	80	74	174:	147		225:	131	117	276:	132	327:	54	41
22:			73:	-25	-33	124:	133	115	175:	134		226:	150	139	277:	100	328:	75	46
23:			74:	2	-8	125:	105	91	176:	131		227:	177	152	278:	95	329:	20	17
24:			75:	-22	-31	126:	87		177:	175	190	228:	187	150	279:	99	330:	16	16
25:			76:	19	22	127:	93		178:	132	200	229:	170	189	280:	131	331:	9	22
26:			77:	31	27	128:	60		179:	104	171	230:	169	177	281:	131	332:	10	18
27:			78:	28		129:	96	91	180:	140	158	231:	164	162	282:	116	333:	18	30
28:			79:	19		130:	89	77	181:	139	156	232:	95	167	283:	95	334:	2	37
29:			80:	36	49	131:	78	71	182:	103	178	233:	110		284:	44	335:		116
30:			81:	29	28	132:	77	72	183:	112	190	234:	79	88	285:	38	336:		130
31:			82:	26	30	133:	89	85	184:	152	154	235:	98	81	286:	45	337:		18
32:			83:	60	20	134:	75	72	185:	145	142	236:	118	100	287:	40	338:	87	65
33:			84:	51	40	135:	38	38	186:	141	150	237:	110	113	288:	75	339:	83	70
34:			85:	31	5	136:	55	39	187:	184	204	238:	120	112	289:	78	340:	46	53
35:			86:	-21	-34	137:	80	56	188:	147	159	239:	114	121	290:	38	341:	38	12
36:			87:	8		138:	101	77	189:	121	131	240:	143	149	291:	47	342:	8	6
37:			88:	27		139:	104	91	190:		113	241:	121	145	292:	78	343:	4	34
38:			89:	13		140:	131	90	191:		137	242:	130	129	293:	93	344:	10	50
39:			90:	25		141:	135	128	192:		176	243:	127	125	294:	67	345:	2	29
40:			91:	47		142:	123	132	193:		168	244:	159	169	295:	47	346:	49	32
41:		-29	92:			143:	127	130	194:		172	245:	156	161	296:	71	347:	49	11
42:		-2	93:			144:	110	117	195:		152	246:	172	180	297:	61	348:	19	17
43:		10	94:		4	145:	99	99	196:		169	247:	161	177	298:	127	349:	30	5
44:	-3	-26	95:		61	146:	101	101	197:		158	248:	136	147	299:	64	350:	40	8
45:	-4	-29	96:		40	147:	117	108	198:	139	131	249:	153	182	300:	71	351:	43	10
46:	4	-13	97:		17	148:	132	118	199:	145	166	250:	131	162	301:	53	352:	29	5
47:	-25	-30	98:		8	149:	122	123	200:	151	165	251:	117	131	302:	63	353:	22	7
48:		-15	99:		16	150:	131	135	201:	149	161	252:	158	166	303:	75	354:	38	6
49:		1	100:		13	151:	129	134	202:	138	151	253:	101	112	304:	96	355:		10
50:		10	101:		22	152:	114	108	203:	131	128	254:	101		305:	61	356:		48
51:		52	102:		12	153:	80	90	204:	111	126	255:	70		306:	66	357:		29
52:		49	103:		10	154:	102	96	205:	108	119	256:	119		307:	86	358:		36
53:	27	16	104:		12	155:		93	206:	101	104	257:	88		308:	68	359:		
54:	-8	-19	105:	36	59	156:		82	207:	140	121	258:	95		309:		360:		54
55:	-15	-24	106:	40	61	157:	64	82	208:	133	119	259:	176		310:	60	361:	66	74
56:	-20	-21	107:	41	61	158:	79	96	209:	157	154	260:	170		311:	79	362:	72	
57:	-46	-42	108:	58	24	159:	91	115	210:	151	139	261:	156		312:	101	363:	29	

DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM	DAY	VL	UMM
7:			54:	100	100	109:		100	160:	99	100	211:	97	93	262:	98	86
8:			55:	99	99	110:		100	161:	98	99	212:	96	90	263:	97	81
9:			60:	100	100	111:		100	162:	97	100	213:	97	95	264:	98	88
10:			61:	100	100	112:		100	163:	98	100	214:	97	90	265:	97	86
11:			62:	100	100	113:		100	164:	95	100	215:	96	97	266:	98	89
12:			63:	100	100	114:		100	165:	90	98	216:	97	94	267:	98	86
13:			64:	100	100	115:		100	166:	100	100	217:	98	98	268:	98	89
14:			65:	100	100	116:	99	100	167:	96	100	218:	97	95	269:	98	90
15:			66:	100	100	117:	93	100	168:	98	100	219:	97	95	270:	97	90
16:			67:	100	100	118:	100	100	169:	98	100	220:	89	85	271:	98	90
17:			68:	100	100	119:	100	100	170:	97	100	221:	96	95	272:	99	90
18:			69:	100	100	120:	100	100	171:	98	100	222:	90	93	273:	100	92
19:			70:	100	100	121:	98		172:	96	100	223:	97	96	274:	98	91
20:			71:	100	100	122:	100		173:	94	99	224:	97	96	275:	98	92
21:			72:	100	100	123:	98		174:	93	100	225:	95	94	276:	97	89
22:			73:	100	100	124:	97		175:	98	100	226:	84	81	277:	98	90
23:			74:	100	100	125:	100		176:	97	100	227:	70	73	278:	98	91
24:			75:	100	100	126:	98		177:	95	100	228:	90	82	279:	97	90
25:			76:	100	100	127:	100		178:	97	100	229:	97	89	280:	97	89
26:			77:	100	100	128:	99		179:	100	100	230:	97	91	281:	70	84
27:			78:	100	100	129:	100	100	180:	97	100	231:	97	88	282:	97	90
28:			79:	100	100	130:	99	100	181:	97	100	232:		91	283:	97	89
29:			80:	100	100	131:	93	98	182:	94	100	233:	95		284:	97	89
30:			81:	100	100	132:	98	100	183:	96	100	234:	97	82	285:	98	91
31:			82:	97	97	133:	99	100	184:	97	100	235:	95	85	286:	95	86
32:			83:	94	100	134:	99	100	185:	97	96	236:	98	91	287:	97	88
33:			84:	100	100	135:	100	100	186:	97	95	237:	100	91	288:	97	90
34:			85:	100	100	136:	91	98	187:	97	96	238:	98	89	289:	97	91
35:			86:	100	100	137:	71	92	188:	98	95	239:	98	89	290:	97	89
36:			87:	100	100	138:	72	90	189:	97	88	240:	97	90	291:	97	86
37:			88:	100	100	139:	96	95	190:	100	89</						

TABLE E-4. THE minimum relative humidity IN VLAARDINGEN AND OMMOORD DURING THE YEAR OF INVESTIGATION (AS PERCENTAGE).

DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM	DAY	VL	OMM
7:			54:	53	58	109:		72	160:	67	68	211:	72	68	262:	78	72
8:			59:	73	77	110:		66	161:	69	82	212:	58	62	263:	57	53
9:			60:	57	59	111:		77	162:	82	62	213:	48	54	264:	75	67
10:			61:	80	78	112:		54	163:	53	63	214:	57	52	265:	61	57
11:			62:	86	84	113:		73	164:	53	61	215:	80	80	266:	65	55
12:			63:	81	79	114:		63	165:	53	60	216:	62	64	267:	63	60
13:			64:	85	82	115:		55	166:	40	50	217:	77	79	268:	65	68
14:			65:	71		116:	42	57	167:	47	54	218:	57	56	269:	63	57
15:			66:	70	74	117:	54	61	168:	67	68	219:	56	57	270:	63	64
16:			67:	76	77	118:	62	69	169:	51	59	220:	57	57	271:	61	57
17:			68:	73	75	119:	68	73	170:	38	47	221:	53	53	272:	64	60
18:			69:	50	56	120:	73	77	171:	61	66	222:	52	53	273:	75	68
19:			70:	77	73	121:	72		172:	55	62	223:	54	55	274:	61	52
20:			71:	63	69	122:	47		173:	38	50	224:	57	59	275:	57	48
21:			72:	62	68	123:	69		174:	45	55	225:	36	44	276:	78	71
22:			73:	59	69	124:	59		175:	53	54	226:	36	37	277:	59	57
23:			74:	52	62	125:	65		176:	39	48	227:	38	38	278:	62	56
24:			75:	53	63	126:	68		177:	40	52	228:	37	34	279:	60	58
25:			76:	79	84	127:	52		178:	53	64	229:	59	58	280:	91	83
26:			77:	77	79	128:	73		179:	75	80	230:	62	57	281:	96	63
27:			78:	64	66	129:	68	74	180:	56	70	231:	56	58	282:	79	70
28:			79:	63	58	130:	57	61	181:	47	58	232:		64	283:	75	64
29:			80:	74	78	131:	47	55	182:	37	45	233:	48		284:	69	60
30:			81:	51	56	132:	47	54	183:	41	46	234:	38	39	285:	66	68
31:			82:	44	49	133:	62	72	184:	58	63	235:	37	37	286:	64	61
32:			83:	38	42	134:	68	77	185:	58	51	236:	48	44	287:	72	69
33:			84:	74	79	135:	57	67	186:	45	48	237:	52	46	288:	80	72
34:			85:	58	66	136:	43	54	187:	56	58	238:	54	54	289:	93	83
35:			86:	77	80	137:	30	43	188:	74	77	239:	45	46	290:	55	58
36:			87:	66	72	138:	37	43	189:	56	57	240:	64	60	291:	55	57
37:			88:	68	68	139:	52	63	190:	49	50	241:	68	64	292:	82	75
38:			89:	46	52	140:	51	57	191:	40	42	242:	75	69	293:	72	68
39:			90:	45	53	141:	56	63	192:	80	80	243:	55	53	294:	72	68
40:			91:	81	83	142:	45	53	193:	68	68	244:	71	68	295:	65	64
41:			92:	73	75	143:	64	73	194:	59	58	245:	78	70	296:	67	62
42:			93:	58	46	144:	81	82	195:	48	52	246:	70	63	297:	60	63
43:			94:	58	72	145:	64	71	196:	78	79	247:	50	57	298:	73	68
44:	69		95:	97	100	146:	38	48	197:	56	53	248:	50	40	299:	50	52
45:	73		96:	65	64	147:	37	42	198:	71	69	249:	77	71	300:	42	44
46:	71		97:	72	72	148:	38	43	199:	66	65	250:	62	55	301:	70	69
47:	73		98:	67	73	149:	61	68	200:	59	72	251:	64	59	302:	52	48
48:	70	73	99:		61	150:	69	73	201:	57	57	252:	77	69	303:	80	75
49:	73	79	100:		60	151:	79	85	202:	62	61	253:	48	43	304:	71	70
50:	93	92	101:		72	152:	81	84	203:	73	73	254:	51		305:	70	63
51:	94	89	102:		79	153:	62	68	204:	55	53	255:	56		306:	88	81
52:	82	85	103:		77	154:	69	68	205:	55	54	256:	59		307:	73	71
53:	70	76	104:		73	155:		62	206:	62	64	257:	40		308:	78	
54:	73	74	105:		88	156:		60	207:	77	71	258:	36		309:	64	
55:	70	72	106:		83	157:	56	46	208:	68	68	259:	68		310:	66	
56:	75	80	107:		70	158:	44	64	209:	82	80	260:	62		311:	63	60
57:	73	73	108:		81	159:	55	72	210:	76	70	261:	77		312:	87	77

LIST OF ABBREVIATIONS

CNSLD	Chronic Non-Specific Lung Disease
FVC	Forced Vital Capacity
VC	Vital Capacity (inspiratory)
FEV _{1.0}	Forced Expiratory Volume measured over one second
FEV _{1.0} % VC	FEV _{1.0} expressed as a percentage of the observed Vital Capacity
MMFR	Maximum Mid-expiratory Flow Rate
$\dot{V}_{\max}$ at 50% VC	Maximum flow at 50 per cent of the observed Vital Capacity
NO	Nitrogen monoxide
NO ₂	Nitrogen dioxide
SO ₂	Sulphur dioxide
ppm	part per million
mg/m ³	milligrams per cubic meter
µg/m ³	micrograms per cubic meter
ECSC	European Coal and Steel Community
MRC	Medical Research Council
TNO	Toegepast Natuurwetenschappelijk Onderzoek (Applied Scientific Research)
WHO	World Health Organization

