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POPULATION-ATTRIBUTABLE RISKS AND THE HEALTH OF THE DUTCH POPULATION

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PREFACE

In November 1993 the National Institute of Public Health and Environmental Protection (RIVM) published a document which describes the current health status of the Dutch population and which contains past trends and, where possible, expected future developments over the period 1950-2010: *the Public Health Status and Forecasts (PHSF) document.* The document is a rearrangement of existing information by the RIVM along the lines of a conceptual model in close cooperation with many other research institutions. The PHSF document is to be used in policy development or policy evaluation by the Dutch Ministry of Welfare, Health and Cultural Affairs. It is the first in a series and has to appear every fourth year.

The Dutch edition of the PHSF document is made up of three parts. *Part I* gives the broad 'story line'. Starting with the formulation of the concept, it goes on to give a summary of the most important data on the current health status and that of the recent past, and on the determinants of this health status, ending with a look at possible future developments and the usefulness of the assembled material for policy development. *Part II* contains various contributions on the health status and its indicators, and *part III* those on the determinants of health status.

Part I of the PHSF is already translated into English. From the *parts II and III* only several contributions are translated into English, 'Population-attributable risks and the health of the Dutch population' is one of them and the subject of this RIVM report. In international literature a lot of attention is payed to this subject. So translation into English seems justified. The report gives a summary and analysis of the available information on population-attributable risks (PAR) in the Netherlands. This is a translation of *part III 4.2* of the Dutch version. The English edition of 'Public Health Status and Forecasts: The health status of the Dutch population over the period 1950-2010' is published by the Sdu Uitgeverij Plantijnstraat, The Hague 1994, under ISBN 90 339 0697 1. This publication can be ordered from Sdu servicecentrum Uitgeverijen, PO box 20014, 2500 EA The Hague, The Netherlands. Telephone: 031 70378 98 80. Or by fax: 031 70378 97 83. The price of Public Health Status and Forecasts is DFL 44.50 (the forwarding not included).

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ABSTRACT

In this report population-attributable risks (PARs) are reported, which quantify the contribution of several determinants (lifestyle factors such as smoking, alcohol consumption, physical activity and dietary factors, as well as biological risk factors such as total serum cholesterol, HDL-cholesterol, blood pressure, glucose tolerance and body mass index) to mortality from a number of chronic diseases (coronary heart disease, stroke, COPD, diabetes and some forms of cancer).

Relative risks and prevalences of risk factors are needed for calculations of PAR's. Relative risks were taken from the international literature and risk factor prevalences (mainly for the age range 20-59 years) were derived from the 1987-1991 Dutch Monitoring Project on Cardiovascular Disease Risk Factors.

Some important assumptions and difficulties in calculating and interpreting the PAR's and PAR like measures are summarized in chapter 2. Chapter 3 contains a description of PAR calculations for a series of determinants, later summarized (chapter 4) from the viewpoints of both diseases and determinants. PAR's for individual determinants ranged from 10 to 90 percent.

From a Public Health point of view, intervention in a determinant which has a moderately strong influence one or more frequently occurring diseases, will lead to more gain in health than intervention in a determinant which has a strong influence on a rare disease. From the results it is clear, that cigarette smoking is the determinant causing the greatest health loss: the prevalence of cigarette smoking is still high (about 40 percent in men and women aged 20-59 years) in the Netherlands. Cigarette smoking influences mortality from a number of indicators (cancer of the lung, larynx, oral cavity and oesophagus, coronary heart disease, stroke and chronic respiratory disorders). Coronary heart disease has the largest number of determinants for which it was possible to calculate PARs. The general conclusion is that for the health problems mentioned in the Netherlands a substantial health gain is at least theoretically possible. As a large part of these risk factors are made up of life style factors there are important individual and collective choices involved in trying to further improve the health status of the Netherlands.

The PARs calculated here for the individual determinants are a simplification of reality, because interactions between determinants have not been taken into consideration.

Mathematical models are now being constructed which take these interactions into account. In addition, more attention will have to be paid to the health gains that may be achieved in old age.

1 INTRODUCTION

In order to be able to assess a quantitative association between a determinant and an indicator, it is necessary to have data on the strength of the association and the prevalence of the risk factor among the population. Such data may be derived from good epidemiological research. Below, estimates are given with respect to a number of extensively studied determinants of cardiovascular disease, cancer and a few other chronic disorders. The determinants in question are ones from the group of endogenous factors (serum cholesterol, blood pressure, glucose tolerance and body weight), and from the "lifestyle" group (smoking, alcohol consumption, physical (in)activity and diet). Some of the data has been taken from other PHSF contributions (*Part III* of the Dutch edition) in which the individual determinants are discussed in more detail. Where necessary, the data available has been supplemented with data taken from the international literature.

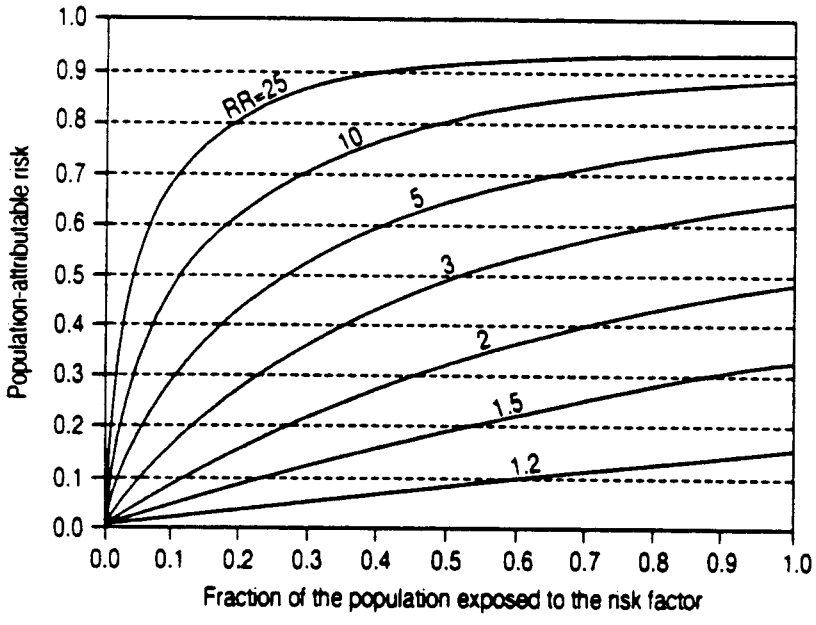
The strength of the association between a determinant or risk factor and the occurrence of the disease is indicated by the relative risk (RR). The RR indicates how much greater the risk of getting the disease is for people who have the risk factor, compared with people who do not. However, a high relative risk does not automatically mean that the health gain to be achieved with respect to the disease by eliminating the risk factor is great. This is also dependent on the occurrence of the risk factor in the population. The health gain which is in theory attainable at the population level can be quantified by calculating the population-attributable risk (PAR). The PAR gives the fraction or the percentage of the number of cases of disease which is attributable to a particular exposure. The PAR can be calculated using the following formula:

$$PAR = \frac{P_e\,(RR-1)}{P_e(RR-1) + 1}$$

where P_e is the fraction of the population in which the risk factor is present and RR is the relative risk for the disease in the presence of the risk factor (see above). The PAR is thus determined by the prevalence of the risk factor and the RR. *Figure 1* shows how, for a given RR, the PAR changes as the prevalence of the risk factor alters.

A PAR gives an estimate of a determinant's contribution to a particular health problem or a particular disease. However, this does not mean that this fraction of the disease can simply be avoided by "eliminating" the determinant. The health gain which is really attainable is determined above all by the extent to which it is actually possible in practice to intervene with respect to a determinant. Here, the term "preventable proportion" (PP) is used. The PP is essentially the portion of the PAR "considered to be attainable in practice". In scenario analyses, various PPs can thus be postulated, associated with different intervention choices. This applies specifically with respect to determinants for which there are more than two risk categories, or for which there is a more or less continuous increase in risk as the level of the determinant increases. It is possible, for example, to calculate the health gain achievable if everyone were to move down by one category (population approach in which the distribution of the entire population shifts), or if only people in the high-risk category (or categories) were to be treated and normalised (comparable with a "high risk" approach). The PARs and also the PPs for a number of determinants are calculated below.

Figure 1: Size of the population-attributable risk (PAR) as a function of the relative risk (RR) and of the prevalence of the risk factor (fraction) in the population.



2 CHOICES AND ASSUMPTIONS

Although the formula for calculating PARs is simple, in practice many methodological problems turn out to arise. A prerequisite for the calculation of a PAR is that the causality of the relationship between the risk factor and the disease has been proved. After all, only then can a health gain be expected from a reduction in the risk factor. Moreover, the PAR does not give any information on the time interval between the fall in the level of the risk factor and the fall in the incidence of, or mortality from the disease. The PAR can therefore be interpreted as a measure which indicates what proportion of the occurrence of the disease is attributable to the risk factor, or what portion of cases of the disease in the future would in theory be prevented in the complete absence of the risk factor.

For the PAR to be calculated, there has to be reliable data available on both the RR and the prevalence of the risk factor in the population (see the formula given). When calculating a PAR for a population, it is implicitly assumed that the RR is equal for all groups within that population. This assumption will not always be correct, for example where there are differences between the young and the old, or between men and women. This leads to distortion of the PAR calculated. However, it is sometimes not possible to calculate age- or sex-specific PARs, either because there is no known data on exposure and/or RRs per subgroup, or because the data which is available on these is less reliable. There has recently been a great deal of debate about the size of RRs among the elderly. For a number of risk factors it appears that the RR in old age is lower than in middle age. Because it is precisely among the elderly that the prevalence of many endogenous risk factors increases sharply, applying too high a relative risk to this group has a considerable influence on the PAR calculated. Because detailed data on prevalence among the elderly is often lacking and the debate on RRs and the effect of intervention in old age is still going on, it was decided to carry out the calculation of PARs in this section separately for men and women, but also to limit the calculation to adults in the 20-60 age group. One exception to this was the determinant (reduced) glucose tolerance, which plays a part specifically in old age, and for which research has been carried out just among the elderly.

In order to calculate a PAR it is necessary to choose from among RR estimates known from the literature, which are often based on foreign research. The RRs presented in the literature can vary somewhat as a result of methodological differences between the studies:

choice of the population investigated, the length of the study, confounding variables, for which corrections have been made (or not) in the analyses, or differences in the level and the duration of the exposure (for example: the effect of smoking is also dependent on the lifetime exposure of the population studied). Uncorrected RRs can also be used, or RRs which have been corrected for a number of confounding variables.

Diseases sometimes have several risk factors which can occur in the same individual in combination, sometimes even more often than might be expected on the basis of the separate figures for the prevalence of these factors (*clustering*) (*see Part III, 4.3* of the Dutch edition). When assessing the RR from risk factor A with respect to disease X, it will be necessary to correct for the occurrence of the other risk factor, B. If this is not done, then it leads to an incorrect estimate of the relative risk from A and thus of the portion of the morbidity or mortality (PAR) which is attributable to risk factor A. In addition, when some risk factors are combined they *interact* - which is to say that the effect of factor A is different when factor B is present from when it is not. A well-known example is the more than additive effect of (combinations of) hypercholesterolaemia, hypertension and smoking. Frequently, however, the prevalence and the risk of the combined occurrence of factors A and B are not known. In the present contribution, PARs have been calculated for determinants separately, with no account being taken of possible interactive effects. In most cases, completely or partly corrected RRs have been chosen rather than uncorrected ones. Sometimes though, corrected RRs were not available, or uncorrected RRs deserved preference. The latter is true in the case of obesity, for example, where it is not useful to correct for intermediaries from the aetiological process for cardiovascular disease, for instance.

Sometimes there will be several estimates of prevalence for the population, for example from different screening programmes. Here again, it will then be necessary to make a choice. The choice of RR and prevalence can have a major influence on the PAR calculated. For this reason and the ones already mentioned, the tables often indicate a *range* of PAR values, based on the lowest and highest estimates of the RR and the prevalence of the risk factor.

Some other aspects which are of importance when assessing PARs relate to the use of a category classification for risk factors which are continuous. For a number of risk factors, such as serum cholesterol and blood pressure, for example, there is no threshold value above which the risk increases; rather the risk increases continuously (linearly or not) with the rise

in the level of the risk factor. A category classification is then often used to calculate the RR. The size of the RR is then heavily dependent on the reference category chosen: the lower the level of the reference category, the higher the RR for a particular higher category. The RR of coronary heart disease for a total cholesterol level of 7 mmol/l is, for example, greater when the reference category (for which the RR is by definition set at 1) is 5 mmol/l than when the reference category is 6 mmol/l. When interpreting the PARs presented it is therefore important to take account of the reference category on which they are based.

To sum up, it may be said that a PAR is calculated using a relatively simple formula, but that the actual interpretation is based on quite a few assumptions and choices. In view of these limitations, the necessary caution should be exercised when interpreting and comparing PAR values with each other.

3 RESULTS OF POPULATION ATTRIBUTIVE RISKS CALCULATIONS

The results described indicate the disorder(s) for which each determinant constitutes a "recognised" risk. It is above all the risk of death (mortality) from the disorder(s) which is involved, and sometimes also the risk of getting the disorder (morbidity). The RRs used come primarily from large-scale, longitudinal foreign studies or from meta-analyses of several epidemiological studies. Prevalence figures for the risk factors (standardised to the 1990 population of the Netherlands) practically all come from the 1987-1991 Monitoring Project on Cardiovascular Disease Risk Factors (Kromhout *et al.*, 1989). The PARs calculated therefore almost always relate to prevalences of the risk factors in the 20-60 age group. The PARs are given as percentages, where possible broken down by sex. Where different studies have produced different relative risks, a range is given in a number of places.

3.1 Smoking

Estimates of the relative risks needed to calculate the PARs are based on an American prospective study (ACS II, Shopland *et al.*, 1991). The relative risks with respect to cancer which were found in this recent study are significantly higher than those in earlier studies (RR for lung cancer: 22 for men and 12 for women), probably because those taking part in the study had smoked longer than those taking part in earlier studies (in which the RR for lung cancer stood at around 10 for men and around 5 for women). The calculation of the PARs was based on the assumption that 40% of men and women were smokers (Monitoring Project on Cardiovascular Disease Risk Factors; *see also Part III, 2.1.2* of the Dutch edition). For smoking, what is particularly striking is the enormous contribution to lung cancer mortality, whereas the PAR for other types of cancer (in the head and neck area) is rather more than 50%. The PARs for mortality from chronic pulmonary disease, coronary heart disease (CHD) and stroke (CVA) are also considerable (*Table 1*).

Table 1: Population-attributable risks of smoking.

determinant	disorder	PAR (%) men	women	range
smoking	CHD (mortality)	42[a]	44[a]	19[b]-42[c] [m]
	CVA (mortality)	52[c]	60[c]	
	cancer (mortality)			
	- lung	90	81	70[d]-90[c] [m] 58[e]-81[c] [f]
	- larynx	79	87	69[f]-79[c] [m]
	- oral cavity	88	66	40[e]-88[c] [m] 28[e]-66[c] [f]
	- oesophagus	73	79	56[f]-73[c] [m] 63[g]-79[c] [f]
	chronic[h] respiratory disorders (mortality)	78	79	78[c]-86[i] [m]

[a] RR used is that for the 35-64 age group

[b] RR (1.6) taken from the MRFIT study (Shaten *et al.*, 1991) for males smoking 1-15 cigarettes per day. The RR from smoking more than 36 cigarettes per day went up to 21.5. RRs corrected for age, ethnic background, plasma triglycerides, diastolic blood pressure, overweight, alcohol consumption, plasma HDL- and LDL-cholesterol, and glucose intolerance

[c] RRs based on ACS II study (US DHHS, 1990; Shopland *et al.* 1991). RRs of CVA for persons aged ≤ 65 (Shopland *et al.* 1991)

[d] RRs based on MRFIT study (Kuller *et al.*, 1991); corrected for age, diastolic blood pressure, serum cholesterol and race

[e] RR based on Cederlof *et al.*, 1975

[f] RR for larynx and oral cavity combined, taken from MRFIT study (Kuller *et al.*, 1991)

[g] RR based on case-control study (Wynder and Stellman, 1977)

[h] Chronic bronchitis, emphysema and chronic obstruction of the airways

[i] RR based on study carried out among British doctors by Doll and Peto (1976)

3.2 Alcohol consumption

A number of health risks are associated with alcohol consumption (*see also Part III, 2.1.3* of the Dutch edition). Thus various studies have found that alcohol consumption increases the risk of haemorrhagic CVA. One of the studies which was stronger from the methodological point of view found that alcohol consumption of one to ten glasses a week among men in the 45-69 age group was already sufficient to give an RR of 2.3 (Donahue *et al.*, 1987). The level of this relative risk has not yet been sufficiently substantiated, however. A lower limit of zero has therefore been kept for the range of the PAR (*Table 2*). There has not yet been enough research carried out with respect to women, and their consumption is too low to make a reliable estimate of the relative risk of CVA.

A great deal of research has been done into the relationship between alcohol consumption and the risk of cancers of the mouth, throat and larynx. However, the studies differ considerably in their definitions of categories of alcohol consumption, characterisation of the reference population (non-drinkers or light drinkers) and confounding variables for which corrections have been made. The minimum estimate of the PAR for men is based on studies in which the relative risk of cancers in the head and neck area was found to be about 2 where consumption was in excess of four glasses per day. In studies in which a higher RR (of around 5) was found for a level of consumption of more than four glasses per day, an elevated RR of 2 was also found at lower levels of alcohol consumption (more than one glass per day). Since the percentage of drinkers consuming more than one glass per day is high, this gives the maximum estimate of the PAR. Studies in which very high RRs were found were disregarded when calculating the PAR. For women, no good estimate can be given, since there has been little research with respect to women, and the research that has been done did not reveal any significantly elevated relative risks (*Table 2*).

Table 2: Population-attributable risks of alcohol consumption.

		PAR (%)	
determinant	disorder	men	women
alcohol consumption (≥ 1 glass per week)	haemorrhagic CVA (mortality)	0-34[a]	?
	cancer of the head and neck[b] area (mortality)	9-33[d]	?
cessation	CHD (morbidity)	-5[d](m/f)	

[a] Reference category: non-drinkers. RR (men aged 45-69), corrected for age, high blood pressure, serum cholesterol, obesity, smoking, uric acid, blood glucose concentration and haematocrit (Donahue *et al.*, 1986)
[b] Source: IARC literature survey (no formal meta-analysis), 1988. Only studies in which corrections for smoking have been made
[c] Cessation of moderate alcohol consumption (1-3 glasses per day)
[d] Calculated as prevented fraction [prevalence times (1 - RR)]. RR = 0.8 (0.7-0.9) (Marmot, 1984)

The relationship between alcohol consumption and the occurrence of coronary heart disease is U-shaped. This means that the relative risk of coronary heart disease in moderate drinkers (compared to non-drinkers) is less than 1 (Moore and Pearson, 1986). For this reason it is not possible to calculate a PAR for alcohol consumption. It is, however, possible to calculate what the effect on health would be if the category of moderate drinkers (1-3 glasses daily, RR = 0.8) were to fall back to a relative risk of 1.0. The protective effect of moderate alcohol consumption which currently exists can also be calculated. This *prevented fraction* (prevalence times (1 - RR)) amounts to around 5% where 25% of the population has a "moderate" alcohol intake. Because a change in the determinant would involve a health loss, the figure calculated is negative.

3.3 Physical activity

Various studies have shown that physical inactivity is strongly associated with total mortality and mortality from cardiovascular disease (*see also Part III, 2.1.5* of the Dutch edition). The population-attributable risk with respect to coronary heart disease is 20% if a relative risk of 2 is kept for the relationship between physical inactivity and the occurrence of coronary heart

disease (Powell *et al.*, 1987) and a prevalence of inactivity of 25% in the Dutch population. This prevalence estimate comes from the Monitoring Project on Cardiovascular Disease Risk Factors, in which "inactivity" is defined as a sedentary or sedentary/stationary occupation plus little physical exercise during leisure time (Kromhout *et al.*, 1989). If the general advice on exercise is adhered to ("exercising at least three times a week for at least half an hour with such intensity that it is only just possible to hold a conversation"), then it is possible that the prevalence of inactivity will rise to 40-60% of the population, with the PAR consequently rising to 30-40%. On the basis of foreign research (Paffenbarger *et al.*, 1977; 1986; Scragg *et al.*, 1987) it may be concluded that the PAR lies between 20% and 50%. The PAR values thus vary somewhat, partly as a result of different definitions of inactivity.

Results from prospective studies are available for calculating the PAR with respect to NIDDM (non-insulin-dependent diabetes mellitus). This PAR is about 10%. This applies for both men and women, after correction for age, overweight, hypertension, smoking, alcohol consumption and cholesterol (*Table 3*).

Table 3: Population-attributable risks of physical inactivity.

determinant	disorder	PAR(%) men/women[a]	PAR(%) range[b]
physical inactivity	CHD (mortality and morbidity)[c]	20	20-40
	diabetes; NIDDM (morbidity)[d]	10	10-20

[a] Based on an RR of 2 and a prevalence of inactivity of 25%
[b] Based on an RR of 2 and a prevalence of inactivity of 25% and 60%
[c] Powell *et al.*, 1987.
[d] Helmrich *et al.*, 1991; Manson *et al.*, 1991; Manson *et al.*, 1992

3.4 Diet

Diet is a complex factor consisting of many components which on the one hand are not easily quantifiable, and on the other may be associated with many different health effects (*see Part III, 2.1.1* of the Dutch edition). Here we shall be looking specifically at the intake of saturated

fat and fruit and the effects of these on health.

Saturated fat

There is a clear correlation between the intake of saturated fat, the total cholesterol level in the blood, and mortality from coronary heart disease. Using Keys' formula (Keys *et al.*, 1965) it is possible to calculate that a fall in the intake of saturated fat in the Netherlands from the present 16% of total energy intake (WVC, 1986) to the 10% of total energy intake recommended by the Netherlands Food and Nutrition Council (*Voedingsraad*, 1986) would lead to a fall in cholesterol level of about 7.5%. Because it has been demonstrated that a 1% fall in cholesterol level leads to a reduction of at least 2% in mortality from coronary heart disease (NRC, 1989; Holme, 1992), a 7.5% fall in cholesterol would result in an estimated fall of 15% in mortality from coronary heart disease (*see Table 4*).

Table 4: Population-attributable risks of diet (saturated fat and little fruit).

determinant	disorder	PAR (%) men/women	range
food intake:			
saturated fat	CHD (mortality)[a]	15	
fruit	lung cancer (morbidity)[b,c,d]	9	9-17

[a] PAR based on a fall in saturated fat intake from 16% to 10% of total energy intake (conversion in accordance with Keys *et al.*, 1965), followed by a 7.5% fall in average total cholesterol level and an estimated 2% fall in mortality (CHD) for each percent fall in cholesterol

[b] RRs taken from Wang Long-de and Hammond, 1985. Corrected for age; RRs for smokers and non-smokers of the same order of magnitude. Classification into 3 categories: fruit eaten 5-7 days/week (reference category); 3-4 days/week; ≤ 2 days/week

[c] RRs taken from Chow *et al.*, 1992. Corrected for age and smoking. Classification: 4 categories: ≤ 30 times/month (reference category); 31-60 times/month; 61-90 times/month; > 90 times/month

[d] RRs taken from Fraser *et al.*, 1991. Corrected for age, sex and smoking. Classification into 3 categories: < 3 times/week (reference category); 3-7 times/week; > once per day

Fruit

There are more and more indications that eating (plenty of) fruit and vegetables reduces the risk of certain forms of cancer. This protective effect has been demonstrated most clearly for lung cancer, and since the evidence for fruit is stronger than for vegetables a "preventable proportion" has been calculated on the basis of the data from several cohort studies (Wang

Long-de and Hammond, 1985; Fraser *et al.*, 1991; Chow *et al.*, 1992), with the assumption being made that everyone moves up by one category. The percentage of lung cancers that can be prevented varies from 9% to 17% (*see Table 4*).

3.5 Serum total cholesterol and HDL cholesterol levels

As the total cholesterol level increases, so does the incidence of/mortality from coronary heart disease (CHD), which follows a continuously rising (curvilinear) relation (Stamler *et al.*, 1986). There are also more and more indications that a low HDL-cholesterol level constitutes an independent risk factor for CHD (Gordon *et al.*, 1989). Estimates of total and HDL-cholesterol levels are based on the Monitoring Project on Cardiovascular Disease Risk Factors (*see Part III, 1.2.2* of the Dutch edition). The relative risks for the total cholesterol level are based on the MRFIT Study (men only) and the Framingham Study (men and women; Stamler *et al.*, 1986; Castelli *et al.*, 1986). The RRs for the HDL-cholesterol level are based on the Framingham Study and the LRC Study (Wilson *et al.*, 1988; Jacobs *et al.*, 1990).

Depending on the study serving as the source for the relative risk, the PAR with respect to CHD for the total cholesterol level varies from rather more than 10% to just under 50%. The lowest estimate, based on the Framingham Study, has been corrected for the other most important risk factors; the highest estimate, based on the MRFIT study, has only been corrected for age, and used ≤4.32 mmol/l as the reference level. In practice, a PAR based on a reference level of 4.32 mmol/l does not appear to be so relevant, since it seems unlikely that it will be possible to bring everyone's total cholesterol level down to this level. Another approach is to calculate what is known as the "preventable proportion" (PP), which involves simulating different variants of fall in the prevalence of the risk factor. When a number of levels of risk are introduced and it is then assumed that everyone moves down by one risk category, then working with the MRFIT data we get PPs of 16% (men) and 15% (women). With the Framingham data we get PPs of 10% (men) and 9% (women). Calculations of this kind are possibly a better (more realistic) approximation of the health gain to be achieved. It seems likely that a 10-15% reduction in CHD (*Table 5*) may be achieved in this way.

Table 5: Population-attributable risks of total cholesterol and HDL cholesterol.

		PAR (%)		
determinant	disorder	men	women	range
total cholesterol	CHD	13[a]	12[a]	13[a]-47[b] [m] 12[a]-45[b] [f]
HDL cholesterol	CHD	45[d]	33[d]	42[c]-45[d] [m] 33[d]-41[c] [f]
	CHD[d]	19[d,e]	13[d,e]	17[c,d]-19[d,e] [m] 13[d,e]-17[c,d] [f]

[a] RRs taken from the Framingham Study (Castelli *et al.*, 1986); corrected for age, systolic blood presure, smoking, BMI, HDL. Reference level: 5 mmol/l

[b] RRs taken from MRFIT study (Stamler *et al.*, 1986); corrected for age. Reference level ≤ 4.32 mmol/l

[c] RRs taken from the Framingham Study (Wilson *et al.*, 1988); corrected for systolic blood pressure, smoking, BMI, age and total cholesterol. Category classification: sex-specific quintiles from Monitoring Project on Cardiovascular Disease Risk Factor. Reference category: ≥ 1.32 mmol/l (men) and ≥ 1.62 (women)

[d] Preventable Proportions (see text) or the more realistic portion of calculated PARs lying above these. The differences in RR between men and women are smaller in the Framingham Study than in the LRC study.

[e] RRs taken from LRC study (Jacobs *et al.*, 1990); corrected for age, LDL-cholesterol, BMI, systolic blood pressure, smoking. Category classification: see (c)

The importance of a high HDL-cholesterol level is also apparent from the table. The PARs for this are high (30-40%) when calculated for an increase in HDL-cholesterol in the total population to levels of 1.32 mmol/l (men) and 1.62 mmol/l (women) or higher. The PP for the HDL level can be calculated by assuming that everyone moves up to the next higher HDL quintile (average increase 0.15-0.2 mmol/l). This PP value is 19% for men and 13% for women (*Table 5*).

3.6 Blood pressure

In calculating the PAR for blood pressure it was assumed that every blood pressure higher than a chosen value could be brought back down to that value. The following cut-off points were chosen: systolic blood pressure 120 mmHg and/or diastolic blood pressure 80 mmHg. A preventable proportion (PP) was also calculated for blood pressure, it being assumed that only "hypertensives" were being treated. The criterion of the "Netherlands Hypertension Consensus" was adopted (*see Part III, 1.2.1* of the Dutch edition). This means that treatment

for hypertension is indicated for a systolic blood pressure of ≥ 160 mmHg. The PP for CHD, working on the assumption that the blood pressure of everyone with a systolic blood pressure of ≥ 160 mmHg should be brought down to 120 mmHg (the category with a blood pressure of between 120 and 160 mmHg thus being left untreated), is around 5 per cent ("high risk" approach). The difference compared with the PAR presented in *Table 6* is explained by the fact that many people in the 20-60 age group have a blood pressure of between 120 and 160 mmHg, and that the prevalence of a systolic blood pressure of more than 160 mmHg is (still) relatively low in this group.

Table 6: Population-attributable risks of blood pressure.

determinant	disorder	PAR (%) men[a]	women[a]	range
blood pressure: systolic blood pressure	CHD (mortality)	30	19	[b]
	CVA (haemorrhagic and non-haemorrhagic) (mortality)	23	25	
diastole	CHD (mortality)	16	9	16[a]-26[c] [m] 9[a]-18[c] [f]
	CVA (haemorrhagic and non-haemorrhagic) (mortality)	10	7	10[a]-31[c] [m] 7[a]-22[c] [f]

[a] RRs taken from the Framingham Study (Dawber, 1980); corrected for age. Reference category: < 120 mmHg (systole); < 80 mmHg (diastole)

[b] PAR (men) is also 30% with RR from MRFIT study (Neaton and Wentworth, 1992); corrected for age; reference category: < 118 mmHg (systole)

[c] RRs taken from meta-analysis (MacMahon *et al.*, 1990); corrected for age, sex, cholesterol, smoking; reference category: < 80 mmHg (diastole).

3.7 Glucose tolerance

The PARs for glucose tolerance were calculated using prevalence figures from the Hoorn Study (Mooy *et al.*, 1992). This involved a population aged 50-75, and the PARs calculated therefore also relate to this age group (*Part III, 1.2.4* of the Dutch edition). The RRs for mortality from coronary heart disease and CVA come from a number of different studies and were calculated for persons with glucose intolerance (reduced glucose tolerance and diabetes

mellitus) compared to persons having normal glucose tolerance. From these PAR calculations it appears that glucose intolerance accounts for around 12-17% of mortality from CHD and 11-23% of mortality from CVA. The contribution to CVA mortality among women turns out to be twice that among men (*Table 7*).

Table 7: Population-attributable risks of glucose intolerance.

		PAR (%)		
determinant	disorder	men	women	range
glucose intolerance[a]	CHD (mortality)[b]	12	17	11-23
	CVA (mortality)[c]	11	23	[d]

[a] Reference category: normal glucose tolerance (WHO criteria, 1985), based on single measurement

[b] RRs: weighted average from several studies: Kannel and McGee, 1981 (lower limit); Pan *et al.*, 1986 (upper limit); Donahue *et al.*, 1987. Corrected for age, systolic blood pressure, smoking, total cholesterol and ECG abnormalities

[c] RRs weighted average from several studies: Barrett-Connor and Khaw, 1988; Feskens and Kromhout, 1992. Corrected for age, systolic blood pressure, smoking, total cholesterol and BMI.

[d] No range calculated owing to lack of data

The relationship between glucose tolerance and cardiovascular disease is probably continuous, i.e. the higher the blood-glucose values, the higher the risk of CHD (Feskens and Kromhout, 1992). In view of the lack of detailed data, for example with respect to women, it was not possible to calculate a PP. *Table 7* therefore gives only PAR values.

Finally, it should be mentioned that the RRs used here have not been fully corrected for overweight, diet or physical activity. This should therefore be taken into consideration when making a final interpretation of the PARs found.

3.8 Body weight

PARs for overweight (obesity) are really only meaningful for diseases bearing a linear relationship to it. In the case of U- or J-shaped relationships (like those between overweight and total mortality and some forms of cancer), an optimum range for Body Mass Index (BMI) (*see Part III, 1.2.3* of the Dutch edition) must be defined. In addition, practically all studies have shortcomings - such as not correcting for smoking and for diseases which affect weight,

or wrongly correcting for intermediate variables. PARs are therefore only presented for diseases and the associated RRs for which the above objections do not apply. The RRs reported in the literature vary considerably as a result of the differences in populations - for example by age or ethnic background. Another problem is that the definitions of "obesity" differ considerably, so that the RRs reported are not always for the desired classification (for example in accordance with the WHO definition).

The PARs calculated here are based on an estimated average prevalence of overweight of 7% for men and 9% for women. In the case of coronary heart disease, the risk is largely from other risk factors (such as hyperlipidaemia and hypertension), which means that correcting for these factors would lead to a substantial reduction in the PAR.

The relative risk of overweight for diabetes can best be estimated on the basis of data from the Nurses Health Study (Manson *et al.*, 1990), because this contains the right exposure categories. On the other hand, this study does give the highest relative risks. A recent survey of 11 prospective studies into the relationships between Body Mass Index (BMI) and diabetes mellitus showed that the studies varied considerably with respect to classification according to overweight, and also with respect to the diagnosis of diabetes (Feskens, 1992). The PARs calculated in that survey lay in the range from 11% to 58%. The PAR calculated on the basis of relative risks taken from the Nurses Health Study thus lies at the end of this range.

For breast cancer, many different relative risks are found in postmenopausal women. In the Nurses Health Study, for example, no relationship was found between obesity and breast cancer. However, the women studied were relatively young (London *et al.*, 1989). Generally speaking, the relative risk increases with age. The range of PARs here could therefore lie between 0 and around 8% (*see Table 8*).

Table 8: Population-attributable risks of obesity.

determinant	disorder	PAR (%) men	PAR (%) women
obesity (BMI ≥ 30 kg/m²)[a]	CHD (morbidity)[b]	13	15
	NIDDM (morbidity)[c]	56	60
	breast cancer (mortality)[d]		8

[a] For all the PARs calculated the following applies: reference category BMI ≤ 25 kg/m² and RRs corrected only for age

[b] RRs taken from Nurses Health Study (Manson *et al.*, 1990)

[c] RRs taken from Nurses Health Study (Colditz *et al.*, 1990)

[d] Only in (late) postmenopausal women. Prevalences of overweight among Dutch women aged 40-75 taken from "Prevention" study (Den Tonkelaar *et al.*, 1992). RRs taken from Tretli *et al.*, 1989

4 CONCLUSIONS

Above an attempt has been made to chart quantitatively the contribution which a number of important endogenous and lifestyle factors make to a number of important public health problems. This was done by calculating population-attributable risks (PARs) on the basis of relative risks (RRs) and the prevalence of these risk factors. As already mentioned under "Choices and assumptions", the necessary caution should be exercised when interpreting PARs. All the PARs calculated are summarised once more in *Table 9*, but this time ranked according to disorder. In this way, both the question "what health problems (indicators) are associated with this determinant?" and the question "what determinants are associated with this health problem?" are dealt with.

Table 9: Summary table of population-attributable risks (PARs), ranked by disease.

disorder (mortality/morbidity)	determinant	PAR (%)		PAR range (%)	
		men	women	men	women
coronary heart disease (CHD)					
CHD	smoking	42[a]	44[a]	19[b]-42[c]	
CHD	total cholesterol	13[a]	12[a]	13[a]-47[b]	12[a]-45[b]
CHD[e]	HDL cholesterol	19[e,d]	13[e,d]	17[e,c]-19[e,d]	13[e,d]-17[e,c]
CHD	diet: saturated fat[a]	15 (m/f)			
CHD	blood pressure (systolic)[a]	30	19	[b]	
CHD	blood pressure (diastolic)[a]	16	9	16[a]-26[c]	9[a]-18[c]
CHD	glucose intolerance[b]	12	17	11-23	
CHD (morbidity)[b]	obesity[a]	13	15		
CHD (mort./morb.)[c]	physical inactivity[a]	20[a] (m/f)			20-40[b] (m/f)
CHD[c]	alcohol consumption (cessation)	-5 (m/f)			
stroke (CVA)					
CVA	smoking	52[c]	60[c]		
CVA (haemorrhagic and non-haemorrhagic)	blood pressure (systolic)	23	25		
CVA (haemorrhagic and non-haemorrhagic)	blood pressure (diastolic)	10	7	10[a]-31[c]	71-22[c]
CVA	glucose intolerance[c]	11	23		
CVA (haemorrhagic)	alcohol consumption (≥ 1 glass/week)	0-34[a]			
chronic respiratory disorders[h]	*smoking*	78	79	78[c]-86[i]	
diabetes					
NIDDM (morbidity)[c]	obesity[a]	56	60		
NIDDM (morbidity)[d]	physical inactivity[d]	10[a] (m/f)			10-20[b] (m/f)
various forms of cancer					
lung cancer	smoking	90	81	70[d]-90[c]	58[c]-81[c]
lung cancer[b,c,d]	diet: fruit	9 (m/f)			9-17 (m/f)
breast cancer[d]	obesity[a]		8		0-8
larynx	smoking	79	87	69[f]-79[c]	
oral cavity	smoking	88	66	40[f]-88[c]	28[c]-66[c]
head/neck area	alcohol consumption (≥ 1 glass/week)	9-33[b]			
oesophagus	smoking	73	79	56[f]-73[c]	63[g]-79[c]

[a-i] The notes match those in tables 1 to 8. Most PARs have been calculated on the basis of the prevalence of risk factors among the Dutch population in the 20-60 age group

4.1 Conclusions from the indicators

* PARs have been determined with respect to four diseases and for several risk factors, namely: coronary heart disease (CHD), stroke (CVA), diabetes (NIDDM) and cancers of the head and neck area;
* for CHD the most important contributions are made by smoking, diet (high intake of saturated fat), high total cholesterol and low HDL-cholesterol levels, systolic hypertension and physical inactivity, to which specifically in the case of women glucose intolerance can be added;
* for CVA the most important contributions are made by smoking and systolic hypertension, to which in the case of women glucose intolerance must be added;
* for cancers of the head and neck area, smoking and excessive alcohol consumption make the most important contributions;
* for NIDDM the most important contribution is made by obesity, followed some way behind by physical inactivity;
* PARs for a single disease can add up to (well) over 100%, as is clear from the case of coronary heart disease. This should come as no surprise, since determinants can be seen as links in a chain of cause-and-effect relationships. The removal of a single link can therefore be sufficient to break through the entire chain. Each determinant which is a necessary prerequisite for the development of a health problem can in theory result in a PAR of 100%. Determinants can also be interdependent (for example diastolic and systolic blood pressure) or be influenced by one and the same underlying factor.

4.2 Conclusions from the determinants

* all the determinants discussed here make an important contribution to one or more health problems, with individual PARs ranging from 10% to 90%;
* there are sometimes substantial margins of uncertainty in the PARs, depending on the relative risks and the definitions of risk factors used;
* high systolic blood pressure contributes more to mortality from CHD and CVA than high diastolic blood pressure;

* glucose intolerance (which also includes diabetes itself) contributes to mortality from CHD and CVA;
* obesity makes a substantial contribution to the burden of disease from non-insulin-dependent diabetes mellitus (NIDDM), but also to the burden from CHD and (postmenopausal) breast cancer;
* smoking makes a very substantial contribution to mortality from lung cancer, cancers of the head and neck area (e.g. oesophagus), and chronic obstructive pulmonary disease (COPD, including asthma); smoking also makes a major contribution to mortality from CHD and CVA;
* regular low consumption of alcohol contributes to the burden of disease/mortality from haemorrhagic CVA and cancers of the head and neck area, but the extent of the contribution is still unclear;
* physical inactivity contributes to the mortality and burden of disease from CHD and to the burden of disease from NIDDM.

From the point of view of public health, intervention in a determinant which influences more than one (frequently occurring) disease results in more gain than intervention in a determinant which has a strong influence on only one disease. To calculate the contribution which various determinants make to public-health problems as a whole and to make comparisons between these contributions, PAR data must be supplemented with data on the size of the various health problems (expressed using one and the same measure, e.g. mortality). Thus a 30% reduction in lung-cancer mortality would have a much greater effect than an equal reduction in mortality from malaria, because in absolute terms lung cancer is a much more important cause of death in the Netherlands than malaria. Similar calculations have been made for a selection of the disorders discussed here in *3.2* of the English edition of PHSF.

The PARs calculated here for the individual determinants are a gross simplification of reality, particularly since it was not possible to take sufficient account of the interactions and causal chains existing between determinants. Even where a PAR gives an accurate indication of the contribution which a risk factor makes to a disease, it still says nothing about the feasibility of a change in the risk factor and the associated health gain. The time frame of any health changes also remains unclear. Efforts are therefore being made to construct

mathematical models for calculating health gain. Such models can incorporate the interrelationships between the various risk factors, and also the time relationships between the reduction in risk and the expected health gain. Models of this kind in any case also place even higher demands on data gathering efforts than the calculation of PARs. This subject is dealt with in more detail in *4.3 and 4.5* of the English edition of PHSF.

More attention will have to be paid to the health gain possibly achievable in old age - an important topic given the increasing ageing of the population. Partly because of major gaps in the data available, however, it has not been possible to deal with this subject here.

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LIST OF ABBREVIATIONS

ACS	American Cancer Society
BMI	body mass index
CHD	coronary heart disease
CVA	cerebrovascular accident
DHHS	Department of Health and Human Services
ECG	electrocardiogram
HDL	high-density lipoprotein
IARC	International Agency for Research on Cancer
LDL	low-density lipoprotein
LRC	Lipid Research Clinics [Prevalence Study]
MRFIT	Multiple Risk Factor Intervention Trial
NIDDM	non-insulin-dependent diabetes mellitus
NRC	National Research Council (Washington)
PAR	population-attributive risk
PHSF	Public Health Status and Forecasts
PP	preventable proportion
RR	relative risk