## Registers in cardiovascular epidemiology

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# General Discussion

The central theme of this thesis is the use of registers in cardiovascular epidemiology. We looked at this broad theme from two perspectives. Monitoring cardiovascular disease using national registers is our first perspective and the possible use of registers in various types of epidemiological research the second. In the discussion of our first perspective, we aim to provide a better understanding of the changing pattern of cardiovascular morbidity and mortality by looking at some significant developments within cardiovascular epidemiology. The specific context of the project offered several opportunities to debate the strengths and limitations of research involving registers with persons from different settings, including treating physicians, registry personnel, statisticians and epidemiologists. These debates have shaped the general discussion on the second perspective: the role of registers in epidemiological research. In the end, some concluding remarks are made integrating the two perspectives.

## First perspective: monitoring cardiovascular disease using registers

The interpretation of the trends in cardiovascular morbidity and mortality in the Netherlands, as described in this thesis, is facilitated by starting with a short overview of the main developments within cardiovascular epidemiology.[1-4]

### Developments within cardiovascular disease epidemiology

Around 1880, infectious and pulmonary diseases were the major causes of death in the Netherlands.[5] The Burial Act of 1869 resulted in a dramatic improvement in cause-of-death reporting in the Netherlands. It designated the start of monitoring causes of deaths in the Netherlands.[6] Physicians reported around 95% of all deaths in the Netherlands at that time. Around 1930, heart disease had become the leading cause of death. The knowledge about major cardiovascular syndromes, such as acute myocardial infarction and sudden cardiac death, was limited at that time. In many cases these syndromes struck unexpectedly, often taking lives at relatively young age.

Large studies, like the Framingham Study[8] and the Seven Countries Study,[9] were started shortly after World War II to investigate the so-called 'epidemic' of cardiovascular disease. These pioneer studies led to the concept of risk factors.[10] Hypercholesterolemia, hypertension and smoking were recognised as major causes of increased risk for cardiovascular disease. Major prevention campaigns were started to reduce the prevalence of these risk factors in the population, hoping that in return the incidence of events would decrease.

Progress was also made in the treatment of patients with heart disease. Among the first contributions was the treatment of ventricular fibrillation by an external defibrillator[11] and the introduction of coronary care units around 1965.[12] The first bypass operations were performed in the 1960s.[13] Subsequent advances in cardiovascular surgery and anaesthesiology meant that more patients could be operated upon and post-operative mortality decreased considerably. Recent years saw the booming use of catheter-based interventions. Each year around 14,800 coronary bypass operations and 14,000 PTCA procedures are performed in the Netherlands,[14] improving and often prolonging the life of many patients with coronary heart disease.

Progress was also made in diagnostic imaging, first by invasive procedures (angiography) and then increasingly by non-invasive methods, like echocardiography and, most recently, magnetic resonance imaging[15] and electron-beam computed tomography.[16]

A host of drugs have been developed to suppress the symptoms of cardiovascular disease or to prevent cardiovascular events in persons at high risk or with established cardiovascular disease. Four areas stand out. First, patients with hypertension can successfully be treated with diuretics and ß-blockers to reduce their risk of stroke and coronary events.[17] Second, aspirin, ß-blockers and ACE inhibitors have proven to be effective drugs in both the initial treatment of acute myocardial infarction and in the prevention of new coronary events in patients with established coronary heart disease.[18-20] Third, effective lipid lowering drugs have been introduced, capable of achieving large reductions in LDL-cholesterol in patients with hypercholesterolaemia. Lowering blood cholesterol decreases the incidence of coronary events and of cardiovascular deaths.[21] Fourth, further progress has been achieved in the treatment of patients with acute myocardial infarction through the use of thrombolytics and/or acute PTCA.[22,23] Prompt administration of thrombolytic agents not only leads to a proportional reduction of 18% in early mortality, but this benefit is sustained up to at least ten years after the initial myocardial infarction.[24]

All these improvements and efforts in primary prevention, in the treatment of acute syndromes and in secondary prevention were not in vain. They have led to a remarkable decline in age adjusted cardiovascular mortality. A helicopter view on the trends in cardiovascular morbidity and mortality is given in the next section.

## Trends in cardiovascular morbidity and mortality: findings and possible explanations

The good news is the ongoing decline in cardiovascular mortality. Since its peak in the early 1970s, age adjusted cardiovascular mortality has fallen by 32% in the Netherlands. The death rate declined in every age and sex group. Lower cardiovascular mortality accounted for 54% of the 3.1 year gain in life expectancy in men and 63% of the 2.7 year gain in women during this period.

Despite several difficulties in the interpretation of trends observed in hospital discharge and mortality data (see second perspective), the following picture emerges. The decline in total cardiovascular mortality was mainly caused by a decline in mortality from coronary heart disease and stroke (see figure). Age adjusted mortality from both diseases has fallen by about 40% since the mid 1970s. However, recent trends in mortality (from 1988 onwards) from these diseases are diverging. While mortality from coronary causes continues to decline, the decline in stroke mortality has slowed down. The ongoing decline in coronary heart disease mortality is most likely related to an improved prognosis of patients with established heart disease rather than to a lower incidence. Especially the introduction of thrombolytic treatment for acute myocardial infarction and the growing attention for secondary prevention measures have contributed to the longer survival of patients with coronary heart disease.[25] Such improvements did not occur in the treatment of stroke patients. In particular, the results of thrombolysis in the acute phase of stroke have been disappointing.[26]

The longer survival of patients with (coronary) heart disease has its price. It has led to a growing pool of 'saved' patients, who are still at an increased risk of developing recurrent coronary events, of other atherosclerotic manifestations and of developing chronic conditions related to the injury of the myocardium, such as heart failure and atrial fibrillation. The rise in the number of cardiovascular hospital admissions in the Netherlands demonstrates this development (see figure). Major increases were seen for chronic coronary syndromes (*chapter 5*), heart failure (*chapter 4*) and atrial fibrillation.[27] Other manifestations of atherosclerosis, like peripheral vascular disease (*chapter 3 and 5*), are also rising, although mainly in men.

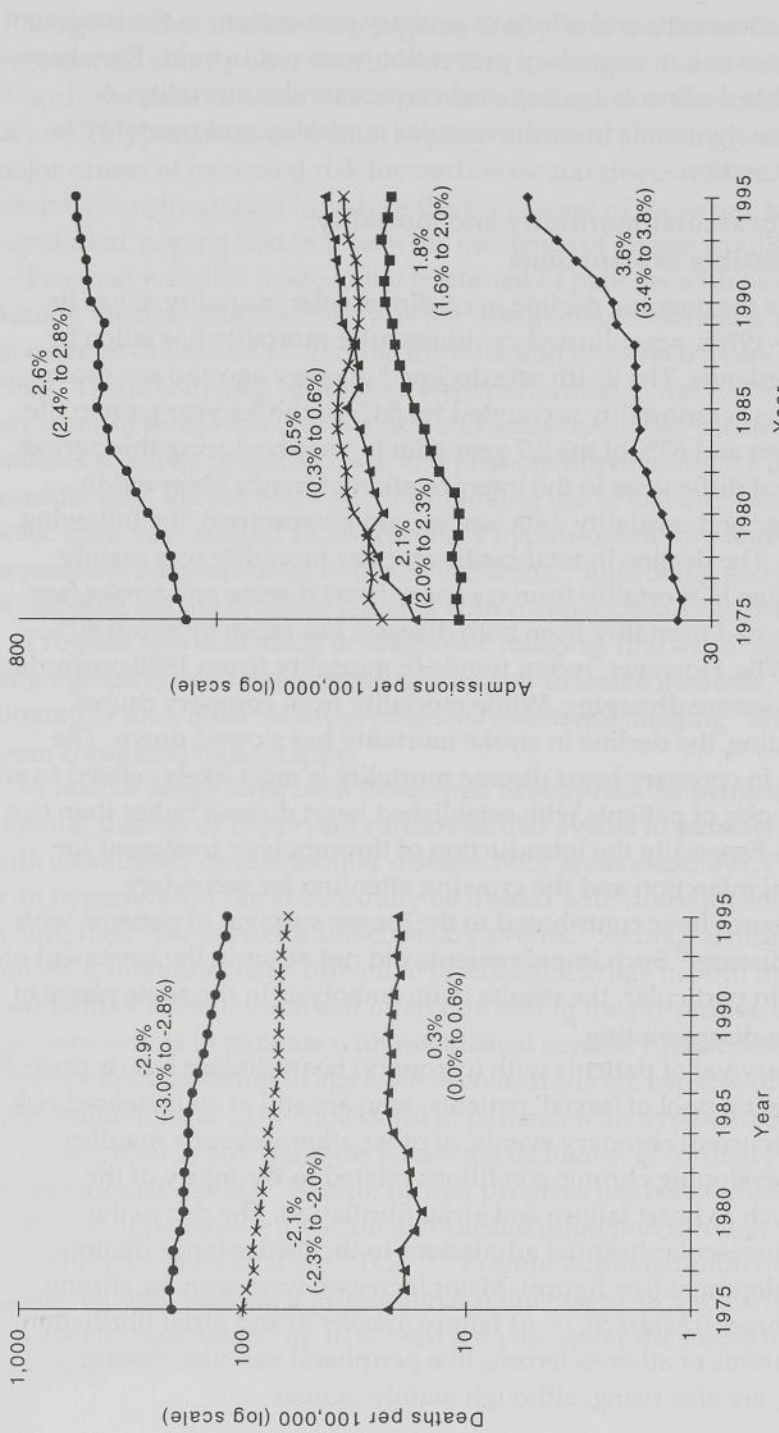


**Figure.** Trends in age adjusted mortality (left) and discharges rates (right) for several cardiovascular diseases from 1975 to 1995 in the Netherlands. ●=coronary heart disease, x=stroke, ▲=diseases of the arteries, ■=heart failure, ◆=atrial fibrillation. Men and women combined. Direct standardisation to the European Standard Population. The annual relative change (95% CI), as estimated by Poisson regression, is presented in the graph. Source: SIG Health Care Information and Statistics Netherlands.

## Prospects for the future

The successful battle against cardiovascular disease has sometimes led to the overoptimistic view among the general public that cardiovascular disease is no longer a major problem.[28,29] This is far from the truth. Cardiovascular disease is still the leading cause of death in the Netherlands and in almost all other Western countries, and will most likely keep that position during the coming decades. It is projected that cardiovascular disease will become for the first time in history the leading cause of death world-wide due to the fact that many developing countries are now adopting Western life-styles, especially in terms of smoking habits.[30] So, despite the impressive decline in cardiovascular disease mortality, the battle is far from over.

Despite our progress in understanding the atherosclerotic process, there are still major gaps in our knowledge.[31] Up to 50% of the patients with coronary heart disease do not have any of the established coronary risk factors (hypertension, hypercholesterolemia, smoking, diabetes mellitus, marked obesity and physical inactivity).[32,33] Although sudden death declined parallel to the decline in total cardiovascular mortality, the overall percentage remains around 40-50%.[34] These include sudden deaths that occur as the first clinical manifestation of unrecognised heart disease and those that occur in patients with known disease of mild-to-moderate severity. These points illustrate that knowledge about vital steps in the process of plaque formation and plaque rupture is far from complete.[35] Promising new therapies are being developed, targeted at several steps in the development of coronary syndromes. They include the prevention of plaque rupture, the prevention of thrombosis, and correcting endothelial dysfunction and injury.

A better understanding of the molecular basis of atherosclerosis may provide further opportunities to fight atherosclerosis.[36] Already a number of monogenic disorders has been identified that are responsible for heart diseases and hypertension. In most cases of cardiovascular disease, there is an interaction between multiple genes and environmental influences. More knowledge about genetic susceptibility will enable physicians to provide individual patients with more targeted prevention measures.

Intriguing new information about cardiovascular disease is still emerging. The observation that babies who are small and light at birth have a greater risk of developing hypertension and hyperlipidaemia, and therefore at higher risk of cardiovascular death (the 'Barker hypothesis'), may provide new insight in the complex process of atherosclerosis.[37] Even the old debate about the role of infections in atherosclerosis has been renewed in the light of new evidence showing the presence of *Chlamydia pneumoniae* in atherosclerotic plaques and

the findings that recent use of antibiotics was associated with lower cardiovascular mortality.[38,39]

However, more knowledge is not everything. Putting what we know into practice has also proved difficult. Several studies have documented that established effective strategies are underused. For instance, blood pressure is inadequately controlled in about 45% of all hypertensives.[40] One third of all patients eligible for aspirin[41] and half of the patients eligible for beta-blockers[42] after acute myocardial infarction do not receive such therapy. Dutch data on many of these points is lacking. The latest trends in risk factors are also worrisome. The number of young people in the Netherlands who start smoking is growing, and so are the number of men and women in our society who lack exercise. There is a growing difference in the prevalence of risk factors between social economic classes, with higher prevalences in lower social economic classes.[43] Current strategies to inform and educate the public need to be adjusted to effectively reach these groups. With respect to primary and secondary prevention we have to be aware that there is a need to lower the prevalence of adverse life-styles at a national level, and not just in high-risk groups alone, the so-called prevention paradox. To use the words of Geoffrey Rose:[44]

> *The prevention strategy that concentrates on high-risk individuals may be appropriate for those individuals, but its ability to reduce the burden of disease in the whole community tends to be disappointingly small. On the other hand, a measure that brings large benefits to the community offers little to each participating individual.*

## SECOND PERSPECTIVE: REGISTERS IN STUDIES EXAMINING TRENDS OVER TIME AND BEYOND

In *chapter 1* we reviewed the interaction between data requirements of various categories of epidemiological research on the one hand and features of the registration process on the other hand. We identified four major sources of problems associated with the use of register data in epidemiological research (see also *section 1.5 and 1.6 of chapter 1*). These sources are:

- the preference of registers to capture conditions with an acute episode leading to health care contact
- the lack of sensitivity and specificity of the registration process
- the lack of historical and prospective information in registers
- the lack of clinical information and/or its inferior quality

The first two sources of problems are of major concern in studies using registers to assess the magnitude of a health problem in the general population or to examine trends over time. The last two sources of problems come into play if registers are used in studies involving temporal relations, like etiological, prognostic and effectiveness studies.

The majority of the studies in this thesis examine trends over time (see *chapters 2 through 5*). This part of the discussion is therefore dedicated to the potential problems of using registers in studies monitoring trends over time. In particular, the focus is on using hospital discharge data and mortality data to monitor cardiovascular disease in the Netherlands. Thereafter, we formulate some general recommendations for the use of registers in epidemiological research.

### Using registers to analyse trends over time

Studies examining trends over time have one particular advantage over studies that try to estimate the true incidence or prevalence of a disease: trends can still be valid despite the fact that not all cases of interest are captured in the register. Trends are particularly valuable if the assumption holds that an observed change in numbers is correlated to a true change in incidence or prevalence of the disease. This reduces the interpretation of changes in register data to one fundamental question: *'is it real?'* Several mechanisms could lead to 'artificial' increases or decreases, not caused by a true rise or fall in incidence or prevalence of the disease of interest. These mechanisms are comparable to the problems encountered in single moment studies, as studies assessing trends over time belong to this category (see *section 1.4 of chapter 1*). The sensitivity and specificity of the registration process with respect to the health

event of interest are the main topics. Sensitivity refers to the ability of a register to capture and correctly classify all events of interest, whereas specificity refers to the ability to exclude non-intended cases. In studies examining trends over time the central question transforms into: *'has there been a change in sensitivity or specificity that could explain the observed trend?'* Possible causes of a change in sensitivity or specificity of the registration process are:

- change in notification behaviour
- change in target population
- change in relation between health event and registration event
- change in classification
- change in coding practice

The first three elements relate to the capturing process of a register, the last two to the recording process (see *section 1.3* and *figure 4 of chapter 1*).

*Change in notification behaviour or in target population*

A change in notification behaviour or a change in target population has a direct effect on the number of cases captured in a register. Fortunately, we did not have to pay much attention to these factors in our interpretation of trends in the number of hospital admissions or deaths.

Notification of deaths is considered to be virtually complete in the Netherlands since 1880, partly because of the legal duty of physicians to report the death of a person.[6]

Notification is a relatively simple process in the case of hospital discharge data in the Netherlands. Local hospital databases are extracted and sent to SIG Health Care information, the holder of the Dutch register of hospital admissions. The odds of missing admissions are remote, given the central role of local databases in administrative functions (including billing). At present, all hospitals in the Netherlands participate in the national register, with the exception of two cancer hospitals and a few specialised hospitals. During our study-period (1972-1995), coverage was incomplete before 1986. We made a general adjustment based on the total number of hospital admissions in the Netherlands, assuming that the pattern of discharge diagnoses in non-participating hospitals was similar to that of participating hospitals.

*Change in relation between health event and registration event*

Here, the situation is different for hospital discharge data compared to mortality data. The decision whether or not to admit a patient highly depends on individual physicians. For example, the number of hospital admissions will fall despite a constant incidence, if more patients are managed on an outpatient basis. In general, there has been a trend towards providing more

outpatient and out-of-hospital care, partially because of constraints on the health care budget.

Improvements in diagnostics capabilities can also influence the relation between disease and admission. Better diagnostic techniques can lead to more admissions, as milder or less advanced cases can be detected sooner and more often. This leads to a change in case mix, which can affect in-hospital mortality rates. Furthermore, improved diagnostics capabilities can lead to more specific coding. We found indications for increased detection rates in the case of abdominal aorta aneurysm through ultrasound (*chapter 3*) and for more specific coding in the case of stroke subtypes through computed tomography (*chapter 2*). The exact impact of changes in hospitalisation rate and/or improvements in diagnostic capabilities is, however, difficult to estimate. These topics return in every discussion paragraph of the studies examining trends over time (*chapters 2 through 5*).

The relation between health event and registration event is different in mortality. Physicians cannot influence death in the same way as they can decide on whether or not to admit a patient. There is an alternative explanation for a decline in mortality besides a decline in incidence: lower case fatality. Evidence from other studies on the prevalence of risk factors and improvements in medical care is often needed to distinguish between lower incidence and lower case-fatality.[25,45,46] We combined the results of several studies to argue that a change in incidence was a more likely explanation for the decline in cardiovascular mortality during the 1970s to mid eighties and that a better prognosis was a more important contributor to the recent decline in cardiovascular mortality (*chapter 5*).

*Change in classification or coding practice*

There has been one change in version of the *International Classification of Diseases* (ICD) during our study-period from 1972 to 1995. The ICD is used in the coding of deaths, and a modification thereof for the coding discharge diagnoses. The ICD-8 version was used from 1972 until 1989 for the death register and until 1990 for the national hospital register. Thereafter, coding was according to the ninth version. This change in ICD version had little impact on the total group of cardiovascular disease, but its impact on specific diseases was noticeable. It was one of the reasons to limit our analysis of heart failure to the ICD-9 period (*chapter 4*).

Several studies have shown that coding errors are fairly prevalent and often related to a lack of knowledge on coding or inherent difficulties in assigning a single cause of death (or discharge) in situations where multiple and related diseases are present.[47-57] Information about changes over time in

coding errors is, however, scarce. A few studies have examined the impact of changes due to new reimbursement systems.[58,59] The ever-falling rate of necropsies in many countries, including the Netherlands,[60] also reduces the possibility to examine changes over time in coding practice using the concept of epidemiological necropsy.[61]

*In summary*

The value of analysing trends over time depends largely on the assumption that a change in trend is related to a genuine change in incidence or prevalence. However, any improvement or deterioration in one of the mechanisms of the capturing or recording process of a register can lead to a change in the number of cases derived from a register.

Our main problem in the interpretation of the decline in cardiovascular mortality was: how much of the decline can be explained by lower incidence and how much by lower case-fatality? Circumstantial evidence from other studies was needed to make inferences.

Our interpretation of trends in discharge data was hampered by the complex relation between the registration event (admission in this case) and the condition of interest. Examples include the shift towards more outpatient and out-of-hospital care and the improved detection capabilities leading to more and milder cases being admitted to hospital. Recurrent events are an additional problem in hospital discharge data compared to mortality data. Trends in (chronic) diseases are difficult to interpret, if multiple events from the same patient cannot be identified. The important distinction between more recurrent events per patient or more new patients cannot be made. Medical record linkage can provide additional insight by recognising recurrent events from the same patient (*chapters 4, 6 and 7*). Medical record linkage and other ways to improve the use of registers are discussed in the next paragraph.

## The use of registers in epidemiological research

Studies using register data are increasingly found in major medical journals. These studies not only address typical public health questions, but clinical questions as well. The attractiveness of large data collections and the growing numbers of registers that routinely collect data from various aspects of health care sometimes leads to the belief that the majority of research can be conducted using registers. This has to be a misconception, as registers are no substitute for primary research. Using registers for all possible research questions is as ineffective as setting up randomised clinical trials in all situations. Dedicated and specified data collection of primary research and the sensible use of registers are complementary methods. The urge to incorporate

more and more information into a register to accomplish an 'ideal' register can even be counterproductive.[62,63] Maintaining such an 'ideal' register would be costly and time-consuming for the providers of the information. The motivation of those involved will quickly fade, and so will the validity of the data. Based on our experiences and the work presented in *chapter 1*, we want to formulate several practical recommendations for a sensible use of registers in epidemiological research.

*(I) Use the natural strengths of registers*

This recommendation is directly related to the dilemma described above. Registers are more suited to answer certain types of questions or to investigate particular diseases.

Studies primarily focussing on the frequency of a health event or studies monitoring changes over time are the most natural ones to be conducted using registers. Under specific conditions, registers can be used in studies involving temporal relations, like prognostic studies, studies examining side-effects, quality of care studies, and comparative studies. The (potential) problems associated with the use registers in various categories of epidemiological research are reviewed in *chapter 1*.

Diseases with an acute episode leading to health care contact and diseases that can readily be diagnosed (simple case definition) are prime candidates to be approached through registers. For diseases or health-related problems outside this category, other population-based approaches are more effective, such as carefully designed health examinations and health interviews.

*(II) Measure and improve the sensitivity and specificity of the registration process*

The sensitivity and specificity of the registration process in relation to specific diseases are essential elements in understanding register data. Important determinants are the number of missed cases and the validity of coding of captured cases.

A key issue in the interpretation of register data is the proportion of cases from the target population that appear in the register (sensitivity or completeness). Independent case ascertainment methods are needed to determine the number of missed cases. There are two common approaches. The first approach determines whether cases identified through death certificates appear in the register, limiting its use to diseases with notable case fatality. The second approach compares the number of cases in the register with the number of cases derived from an independent survey. The comparison with an independent survey is probably the most accurate method for determining

the sensitivity of register, but an expensive one. Other sources that may be used to detect missed cases are biochemical test results (e.g. bacterial cultures, heart enzymes), diagnostic images, ECG readings, biopsies, and prescribed medication.

On-site chart review should be done more frequently in research projects to obtain additional information, to check the validity of key variables and to detect missing information. The validity of the coding process for different diseases can be appraised by such reabstraction methods. In this approach, records that appear in the register are reabstracted at the primary collection site and then compared to the register record. The extent of agreement between the locally reabstracted records and register records is the measure of validity, assuming that the reabstracted records are correct.

*(III) Integrate registers with primary research*

There are two ways to integrate registers with primary research. In the first approach, the register is used as a sampling frame for cases and/or controls. Traditional epidemiological techniques are then applied to collect the data. Both cohort and case-control studies can use this approach. A potential advantage is that the results can readily be generalised to the whole population included in the register. This approach combines the advantage of additional dedicated data collection with one of the strengths of registers, the information on a large number of consecutive cases.

The use of registers in the detection of outcome events in large clinical trials or in population-based cohorts (health interviews or examinations) is the second approach. The national register of causes of death can potentially provide complete information on the number and causes of deaths (ICD codes). Augmenting existing registers with mortality data should be considered for every register in the Netherlands. Hospital discharge data can also provide valuable follow-up information, if the outcome of interest is associated with a moderate to high hospitalisation rate.

*(IV) Use registers to create longitudinal data*

The interest in longitudinal data is growing. The longer survival of patients with heart disease leads to a growing pool of patients at increased risk of recurrent events and of developing other diseases. To study the complex interaction between diseases requires longitudinal data.[64] Registers can provide longitudinal data in two ways. The first way has been described above. It involves the use of registers in providing outcome information in patients from existing cohorts. The second way involves the combination of information from two or more registers or the reconstruction of an event-

oriented register into a patient-oriented register. The national hospital register in the Netherlands is such an event-oriented register. Readmissions from the same patient cannot be identified. This denies the use of discharge data in analysing recurrence rates after an initial event, in determining the risk of developing chronic conditions after acute events, and in the detection of early and perhaps preventable readmissions shortly after discharge.

Longitudinal data requires the identification of patients within and across registers. Ideally, this calls for the use of nation-wide unique identifier (a national health care number). Although Scandinavian countries have demonstrated the value of such a national health care number without compromising the privacy of its inhabitants,[65,66] the introduction of such a number in the Netherlands is not to be expected in the near future. Till then, record linkage can provide a solution (*chapters 6 and 7*).

*(V) Add a few clinical items to administrative registers*

The inclusion of a simple measure of functional health at admission and at discharge would greatly enhance the value of hospital statistics data. Research into developing such a measure is underway.[67]

A limitation that needs urgent attention is the inability to distinguish co-existing conditions present on admission from complications occurring during the hospital stay. If a patient is coded at discharge as having pulmonary embolism, it is impossible to determine whether this happened some time before admission or during the stay in hospital. This difference is vital in studies focusing on quality of care measures.

A variable that indicates whether it is a first episode or a recurrent one is valuable addition in chronic diseases, whereas a variable indicating which side (left, right, both sides) is affected is helpful in diseases that can affect one or both sides.

## CONCLUDING REMARKS

Cardiovascular disease remains a major health problem despite a drop of 32% in age adjusted mortality since the early 1970s. The lifetime probability of dying from cardiovascular diseases, based on current death rates, is still 39% for men and 41% for women. Coronary heart disease and stroke were the major contributors to the decline in cardiovascular *mortality (chapters 2 and 5)*. Mortality from coronary causes continues to decline at the same or even at a higher rate (*chapter 5*) as before, most likely induced by the recent improvements in the treatment of patients with acute myocardial infarction. The decline in stroke mortality on the other hand has slowed down (*chapter 2*).

Increases in age adjusted hospital admission rates are the other side of the cardiovascular picture (*chapters 3, 4 and 5*). Admissions for the work-up and treatment of patients with coronary syndromes, for heart failure and for atrial fibrillation are the main causes for the rise in hospital morbidity. These findings, lower mortality, but more patients with chronic conditions, are signs of a changing profile of cardiovascular disease. Cardiovascular disease is changing from an acute disease with high case fatality into a chronic state epidemic, as illustrated by the rising prevalence of heart failure and atrial fibrillation.

This changing profile has two important consequences. First, the longer survival of patients with heart disease generates new questions about the long-term consequences following the initial manifestations of heart disease. What are the long-term consequences of the growing pool of patients in which death has been postponed by the successful treatment of acute myocardial infarction? Longitudinal data are required to address the dynamic and complex interaction between related and seemingly unrelated diseases. A second consequence of the growing number of patients surviving their acute episode is the need for describing post-event health states. Other measures of health beyond one month or one year survival rates are needed to describe the burden of chronic health states. To adequately measure the burden of chronic diseases, it is necessary to include non-fatal outcomes as well. Several research projects on composite health measures, such as disability adjusted life years, are under way.

Registers themselves have to adapt to this changing profile of cardiovascular disease, although their role in monitoring major cardiovascular morbidity and mortality at a national level will remain a vital one. A new challenge is the use of registers to provide longitudinal data, as we have done in this thesis (*chapter 7*). Registers can be used to provide outcome information

in existing cohorts or the information from several registers involving various health care contacts can be combined to create longitudinal care profiles (the book of life concept).[68] The use of registers to reveal longitudinal information, and by that valuable epidemiological insight, requires the application of medical record linkage techniques (*chapter 6*), as a national health care number is absent in most countries.

Combining information from different sources to answer research questions that were not originally intended, raises important ethical concerns.[69,70] Given the nature of the research, consent was not obtained from the patients involved. The European Union has made a proposal to protect individuals with regard to the registration in databases, including the demand to be notified when data are used.[71,72] Several medical researchers have written about the consequences of introducing such procedures, which can form a serious threat to research using register data.[71,73,74] More attention should be given to the other side of the picture. Is it sensible, or even ethical, that many important questions remain unanswered because we are not making the best use of available data? Clear and well thought general rules are necessary to ensure that important health questions can be answered, but at the same time protect the individual. Such policies can often be established, as the primary interest of epidemiological research is in groups rather than in individuals.[74-76] The urgency to develop clear privacy concepts and derived rules to protect the privacy of individual patients will grow with the increased use of electronic databases.

Physicians and epidemiologists have to learn about this changing profile of research and the possible role of registers herein. Research using these data sources needs the same rigour in design and analysis as other types of research. Teamwork involving epidemiologists, physicians, registry personnel, and statisticians is needed to avoid mistakes and to maximise the use of data from registers.

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